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14. ABSTRACT
In the period covered by this application we have standardized an efficient methodologies for isolating cells from primary tumors expressing RFP by fluorescence activated cell sorting (FACS) and by laser capture micro-dissection (LCM). We have completed a comprehensive micro-array based bioinformatics effort to identify genes whose expression is modulated by Casodex to characterize the molecular events underlying the effects of Casodex on AR+ cell lines (LNCaP and PC-346C cells) The changes in gene expression detected by micro-array were validated by QT-PCR using SYBR green. The results of these experiments are also being compared to the changes in gene expression seen in the PC-346RFP primary tumors (and metastases) from animals chronically treated with Casodex. We have also demonstrated that there is a threshold dose response to Casodex in these cell lines. Results of the dose response revealed considerable differences in expression changes of target genes between Casodex treatments of 50 or 100µM in comparison to control. One of these genes, the cell cycle inhibitor p21 which has been recently shown to have multiple transcript variants also demonstrates differential regulation of the transcripts at the two concentrations. One of the variants, p21B, has been implicated in apoptosis and displays upregulation at concentrations of Casodex that induce cell death. Ingenuity pathway analysis suggest that this gene may be dually regulated by p53 and AR at the higher dose of Casodex.

15. SUBJECT TERMS
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Introduction

In 2000, an estimated 180,4000 men were diagnosed with prostate cancer in the United States, and 31,400 succumbed to the disease (American Cancer Society Facts and Figures, 2000). Due to the increase in public awareness and the greatly increased use of Prostate Specific Antigen (PSA) for screening, prostate cancer now is the second most commonly diagnosed male cancer in many western countries after lung cancer. The major risk factors for prostate cancer include age and race, and the consumption of a high fat diet. The main cause of death from prostate cancer is the invasion and metastasis of prostate cancer to the bone, liver and brain. However, for many men (approximately 100,000 of those diagnosed each year) the disease will remain localized and slow growing. Extensive PSA screening programs have lead to the increased identification of early stage (A1 and A2) tumors in younger men. Approximately 70% of these tumors are indolent and will not need treatment during the patients life time (Choo et al., 2002). Unfortunately at present there is no way to distinguish between aggressive, clinically significant tumors that need to be treated and indolent tumors. As a result, many patients are treated more aggressively than is necessary.

There are four major strategies for treatment of localized, early stage prostate cancer: radical prostatectomy, radiation therapy (either external beam, three dimensional conformal therapy or brachytherapy), hormone therapy (usually with Casodex or flutamide with or without an LH-RH agonist such as Zoladex) and watchful waiting (waiting for the PSA levels to rise before deciding on a course of treatment). The combined five year survival for these interventions is approximately 75 %, however the majority of recurrent tumors develop resistance to further therapeutic intervention. The recent Bicalutamide 150mg (Casodex) Early Prostate Cancer (EPC) Program was established to examine whether adding 150mg/day Casodex immediately to standard care (watchful waiting, radical prostatectomy or radiotherapy) reduces the risk of disease progression and improves survival when compared to standard care alone. Analysis of the data from the EPC Program, which enrolled 8,113 patients with localized and locally advanced prostate, shows that Casodex cuts the risk of disease progression by almost half in patients with localized or locally advanced prostate cancer, and also demonstrates that the time to prostate-specific antigen (PSA) doubling was significantly delayed in patients receiving Casodex and standard care compared with standard treatment alone (Wirth et al., 2001; Wirth, 2001; Iversen et al., 2002). As a result, there is a very significant increase in the number of patients being treated with Casodex, either alone or immediately after surgery or radiation. Furthermore, neoadjuvant therapy with Casodex to debulk organ-confined prostate tumors (particularly stage B1) and to improve positive margins is now widely used prior to surgery and radiation therapy (Padula et al., 2002), and many 'at risk' men (defined as men with two first degree relatives with prostate cancer) are now considering chemoprevention in the form of Casodex (Trump et al., 2001; Schellhammer, 2002).

The aim of the studies funded by this award is to examine the effects of Casodex and other anti-androgens on the induction of apoptosis in androgen dependent PC-346C and LNCaP human prostate cancer cells, and to understand the molecular basis of tumor progression. These cell lines are being used as a model of early, organ confined androgen dependent prostate cancer. One of the major unresolved issues in the development of prostate cancer is the mechanism underlying the progression from hormone dependent to hormone refractory prostate cancer after treatment with anti-androgens. Since there are an increasing number of men being treated with Casodex mono-therapy for localized prostate cancer, as a result of the initial success of the 150mg (Casodex) Early Prostate Cancer (EPC) Program, it is important to fully evaluate the biological effects of Casodex to ensure that it does not induce adverse effects.

Body

The experimental aims for this operating grant are:

Task 1: Analysis of PC-346C cells (months 1-8) to determine the effects of Casodex on apoptosis and cell cycle, determine whether Casodex or flutamide can induce an invasive phenotype, to monitor changes in gene expression using RT-PCR and to clonally expand the invasive cells for further study. Completed.

Task 2: Determine the metastatic capability of the invasive cell lines produced above, both in vitro and in vivo using the orthotopic xenograft model system. (months 8-20). Completed

Task 3: Examine the induction of the invasive phenotype in LNCaP^{GFP} and PC-346^{RFP} cells, and to characterize the changes in gene expression induced by Casodex. (months 8-20). Completed

Task 4: Identify differentially expressed genes using microarray technology (months 3 -36) Completed

With respect to **Task 1**, the experiments have been completed on schedule, and we have written two manuscripts (Zhan et al., 2003 and Lee et al., 2003) that have been published since the last annual report. (See appendix 1 and 2). Briefly we have shown that Casodex induces cell death via an intracellular signaling pathway that is distinctly different from the mechanism of action of TNFα. Treatment of androgen sensitive, non-metastatic LNCaP human prostate cancer cells with 0-100 μM Casodex or 0-10 ng/mL TNFα induces cell death in 20-60% of the cells by 48 h in a dose dependent manner. However, Casodex does not induce classical DNA fragmentation to oligonucleosomes typically induced by TNFα, but rather induces cleavage to form intermediate 60 kb DNA fragments. RT-PCR based analysis demonstrates that in LNCaP cells Casodex coordinately alters the expression of steady state level of mRNAs of several matrix metallo-proteases and their cognate inhibitors (most notably MMP-2 and TIMP-1). Zymography and reverse zymography confirm that the ratio of metallo-protease(s) to inhibitor(s) is altered in favor of activation of the proteases. In cells treated with TNFα, this is accompanied by the loss of mitochondrial membrane potential (ΔΨm) and cell adhesion. In contrast, cells treated with Casodex display loss of cell adhesion, but sustained mitochondrial dehydrogenase activity. Over-expression of Bcl-2 in LNCaP cells attenuates the induction of cell death by TNFα but not Casodex, suggesting that mitochondria depolarization is not required for the induction of cell death by Casodex. While TNFα induces release of cytochrome c in LNCaP cell is associated with the translocation and cleavage of Bax, Casodex-induced cytochrome c release involves both Bax-dependent and -independent pathways, suggesting that Casodex induces cell death by acting on components downstream of decline of ΔΨm and upstream of cytochrome c release. Furthermore, while induction of both caspase-3 and caspase-8 activities are observed in TNF-α and Casodex-treated cells, a novel cleavage product of pro-caspase-8 is seen in Casodex-treated cells. Taken together, these data support the hypothesis that Casodex induces cell death in an indirect and incomplete fashion that is independent of changes in ΔΨm and Bcl-2 actions and results in an extended lag phase of cell survival that may promote the induction of an invasive phenotype after treatment. Thus, different drugs may induce cell death in the same cell line through different mechanisms that involve many or all of the same components of the apoptotic machinery, but with substantially different time course and efficiency. In a small percentage of the treated LNCaP cells, the activation of the ECM-proteases by Casodex also induces an invasive phenotype. The acquisition of an invasive phenotype is not seen when LNCaP cells are treated with TNFα, and is not seen when the LNCaP cells are treated with both compounds simultaneously, suggesting that the phenomenon may be specific to particular classes of compounds. These experiments offer a mechanistic explanation for the failure of most anti-androgen therapies in prostate cancer

and the emergence of hormone refractory tumors that have high propensity for metastasis, and raises questions about the use of Casodex and other anti-androgens for neo-adjuvant therapy or as chemopreventive agents (Zhan et al 2003; Lee at al., 2003)

With regard to the experiments outlined in **Task 2**, we have found that the LNCaP sublines, l-1 and l-33, when grown as xenografts in nude mice grow slowly as well encapsulated primary tumors that metastasized infrequently to other organs (4/50 animals for each subline). We first isolated these cell lines from the invasive LNCaP population that transversed the 8μ membranes in the Boyden chamber assay. *In vitro* these cell lines grow rapidly and are consistently very invasive, however in the xenograft model these cells form relatively slow growing tumors and do not appear to be particularly aggressive. There are possible reasons for this low rate of metastasis: First, in contrast to their invasive phenotype in vitro, these cells may not be intrinsically metastatic in vivo. If the invasive phenotype is not merely an in vitro artifact, this would suggest that the acquisition of an invasive phenotype is reversible and is dependent on either intrinsic or extrinsic signaling to maintain the invasive phenotype. This signaling is presumably not active in the xenografts, or is overridden by other (extrinsic) factors. These factors may include the growth factors present in the Matrigel used during the inoculation of the cells into the mammary fat pad. Secondly, it is well established that the mutation of the androgen receptor present in the LNCaP cells renders the receptor promiscuous, and results in the agonistic activation of the receptor by the adrenal steroid dehydroepiandrosterone (DHEA), which is produced in milligram quantities by the rodent adrenal gland. This agonistic activation of the AR may block or severely blunt the signaling by Casodex that leads to the initiation of apoptosis and metastasis. These two issues appear to confound the successful completion of this task using the experimental approaches initially proposed. However to circumvent these problems we have performed an additional experiment that deviates slightly from the original SOW. The description of this experiment, which utilizes the PC-346C^{RFP} cells has been included under **Task 3b**, and essentially utilizes this new cell line to test the hypothesis that treatment with Casodex induces metastatic progression.

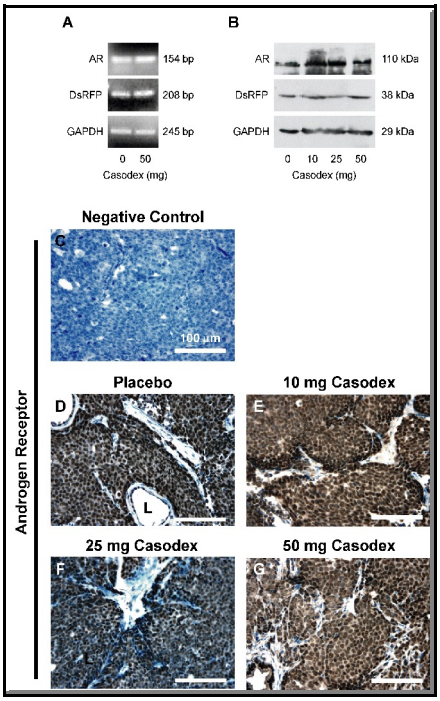


Figure1: Expression of AR in PC-346C^{RFP} tumors treated with Casodex. Panel A: RT-PCR of AR mRNA compared to GAPDH and RFP mRNAs. Panel B: Western analysis of AR expression compared to RFP and GAPDH. Panel C: Immunohistochemistry of AR in tumor cells treated with increasing doses of Casodex. androgen

Task 3a: We have created stable PC-346C cell lines expressing red fluorescent protein RFP (PC-346C^{RFP}) by limiting dilution after transfection with a RFP expression vector and selection with G418. These cell lines undergo cell cycle arrest and apoptosis in a time and dose dependent manner in response to Casodex that is essentially indistinguishable fro the parental cell line. These cells have been used to establish an orthotopic xenograft model of localized prostate cancer expressing the wild type androgen receptor that responds to Casodex treatment in doses that are equivalent to those produced the 150 mg Casodex. We have demonstrated that implantation of Casodex (50mg sustained release 90 day pellets) into androgen replete nude mice induces significant

tumor regression, through cell cycle arrest and apoptosis, and induces significant changes in angiogenesis in the primary tumor. When grown as orthotopic tumors however, these cells do not appear to metastasize after treatment with Casodex. Using Laser Capture Micro-dissection (LCM) and Fluorescence Activated Cell Sorting (FACS) to purify the PC-346C^{RFP} cells from tumors. Using reverse transcriptase polymerase chain reaction (RT-PCR), Western analysis and immunofluorescence we have shown that the expression of Red Fluorescent Protein (RFP) is unaffected by treatment with Casodex (data not shown). Furthermore, even though the tumors undergo significant regression, the expression of the AR in the remaining tumor is essentially unaffected, either in its level or nuclear localization. This is in marked contrast to the in vitro data that has shown that expression of the AR is decreased in both LNCaP and PC-346C cells after treatment with Casodex and the receptor is relocalized to the cytoplasm (Lee et al., 2003).

Task 3b: To determine whether the presence of high levels in the Matrigel used for inoculation affect the metastatic progression of the PC-346C^{RFP} tumors, we have implanted PC-346C^{RFP} cells into the prostate of nude mice in growth factor deleted Matrigel. The PC-346C^{RFP} cell line has a wild type androgen receptor that does not bind to DHEA, obviating the problems with the mutant androgen receptor in the LNCaP. The growth of these cell lines in androgen supplemented nude mice is virtually identical to the growth of the cells in growth factor replete Matrigel, and these tumors also respond to treatment with Casodex (50mg sustained released 90 day pellets), regressing more rapidly tumors established with growth factor replete Matrigel, and showing signs of metastatic progression to the lymph nodes, epididymis and subcutaneous sites, as evidenced by the presence of RFP staining in the metastatic deposits (Figure 2). This pilot study utilized 5 animals for each of the experimental groups, and even though 3/5 animals developed metastases in one or more sites was not large enough to reach statistical significance. As described below (Task 3b, part 2), this experiment was repeated with a modified experimental design using 15 animals per group, and several time points to ensure robust analysis.

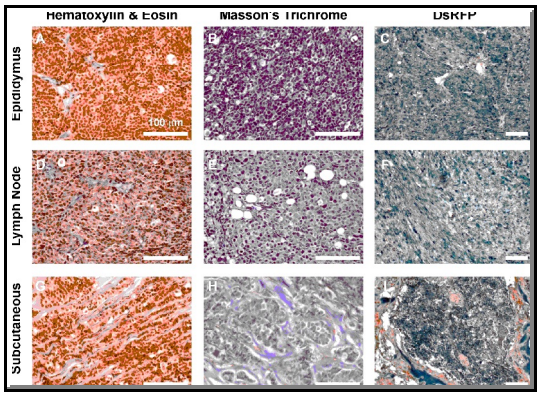


Figure 2: Morphology of metastatic deposits expressing Red Fluorescent Protein(DsRFP).

Task 3b part 2 Repetition of in vivo study to determine whether Casodex induces invasive phenotype secondary to induction of apoptosis.

In the repeat experiment 105 animals were orthotopically injected with 10,000 PC-346C^{RFP} cells/animal in growth factor reduced Matrigel. After three weeks, the animals were randomized into groups of 15 prior to initiation of treatment. One control group was sacrificed at time zero, and the remaining groups were implanted with Casodex (50mg sustained released 90 day pellets) or placebo pellets, and sacrificed at 4, 8 and 12 weeks of treatment. These animals were necropsied, and primary tumor tissue was excised, processed for RNA and protein extraction as well as histopathology. Other organs (lymph nodes, lung, liver and brain) were excised and processed for

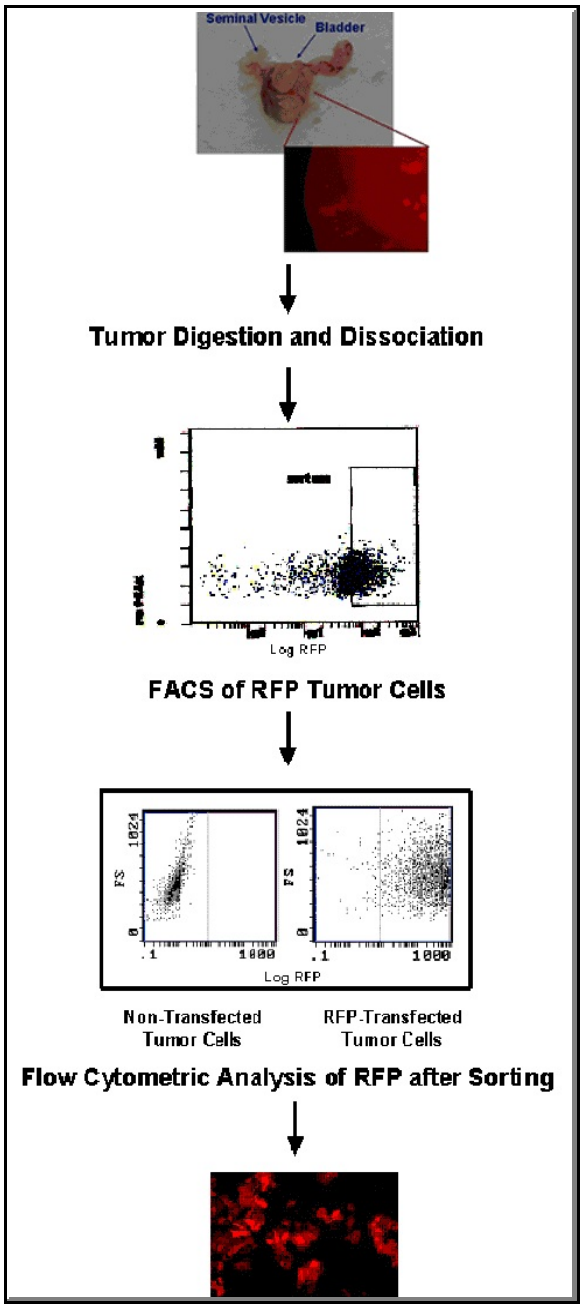


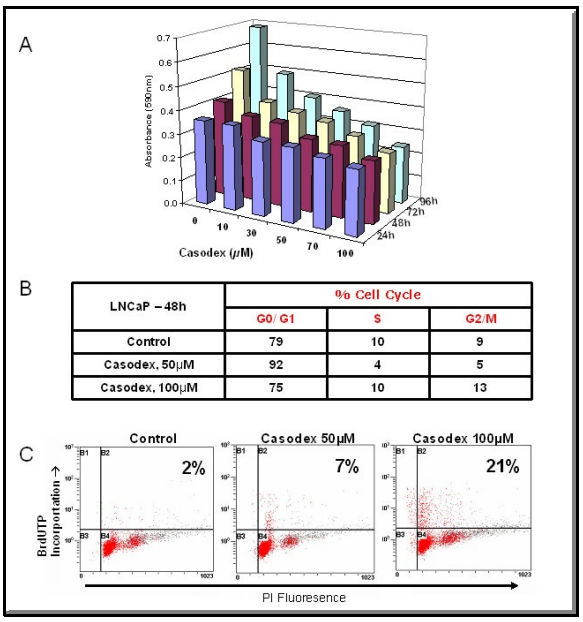
Figure 3: FACS -based purification of PC-346C ^{RFP} cells.

gross pathology and immunohistochemistry for evidence of metastatic dissemination of RFP tagged cells. Primary tumors were sectioned and stained by BrdU and TUNEL to assess the effect of Casodex on cell proliferation and apoptosis. This dose of Casodex induces a substantial slowing of tumor growth, through a combination of cell cycle arrest and apoptosis.

Task 4: We have established the protocols needed for the preparation of RNA for gene array from samples prepared from frozen orthotopic tumors before and after treatment with Casodex. To facilitate these experiments and eliminate variability due to tumor composition which would confound the data analysis, we have developed a very efficient methodology for isolating the human prostate cancer cells from the primary tumor (where they may be contaminated with host stroma), and from metastatic sites (where they may be contaminated with both host stroma and epithelium). This methodology is based on Fluorescence Activated Cell Sorting (FACS) as outlined in Figure 3. This involves dicing the tumors into 1 mm fragments and incubated with CTC (1% collagenase, 0.1% trypsin and 1% chicken serum to dissociated the epithelial cells of the tumor (Montpetit and Tenniswood, 1989), prior to cell sorting on a Beckman-Coulter ALTRA FACS. As outlined in Fig. 3, this methodology has been used to purify PC-346C^{RFP} cells to greater than 98% purity, a purity that is suitable for planned gene array studies. During the course of a 2 hour sort, >500,000 PC-346C^{RFP} positive cells can be purified, providing enough material for RNA and Western analysis. However from our recent experience with gene array, it became clear that the integrity of the RNA from these samples would require at least 7 replicates for each treatment, which would be exorbitantly expensive. We therefore decided to define a panel of candidate genes to be analyzed using Real time PCR (RT-PCR) by defining the array of genes that are altered in response to Casodex in of PC-346C and LNCaP cells in vitro.

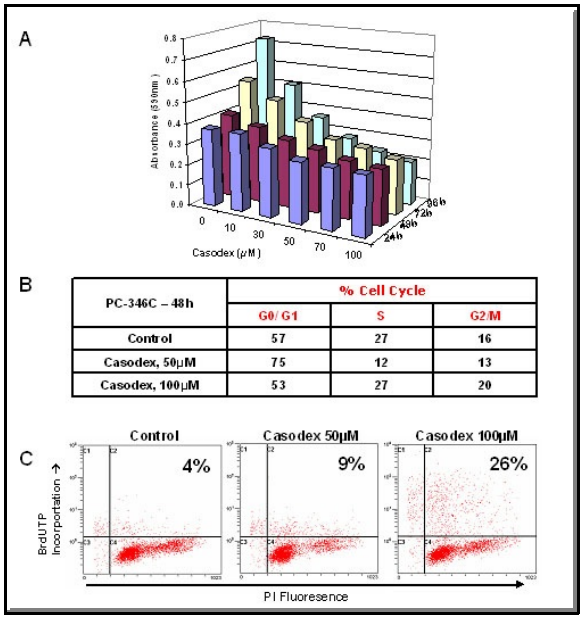
Task 4b. Casodex induces growth arrest and apoptosis in LNCaP and PC-346C cells

We have compared the responses of LNCaP cells (Figure 4) and PC-346C cells (Figure 5) to increasing concentrations of Casodex, which mimic the *in vivo* serum concentrations in the



LNCaP – 48h	% Cell Cycle		
	G0/ G1	S	G2/M
Control	79	10	9
Casodex, 50μM	92	4	5
Casodex, 100μM	75	10	13

Figure 4 – Effect of Casodex on growth and apoptosis of LNCaP cells. LNCaP cells were plated on 24-well plates and treated with 10-100μM Casodex for 24-96h. Adherent and surviving cell were analyzed by crystal violet assay (A). The effects of 50 and 100μM Casodex after 48h treatment on cell cycle kinetics and apoptosis were evaluated by flow cytometry. DNA content was detected using propidium iodide staining (B) and DNA fragmentation by analysis of Apo-BrdU incorporation (C). Results are representative of 3 independent experiments.



PC-346C – 48h	% Cell Cycle		
	G0/ G1	S	G2/M
Control	57	27	16
Casodex, 50μM	75	12	13
Casodex, 100μM	53	27	20

Figure 5 - Effect of Casodex on growth and apoptosis of PC-346C cells. PC-346C cells were plated on 24-well plates and treated with 10-100μM Casodex for 24-96h. Adherent and surviving cells were analyzed by crystal violet assay (A). The effects of 50 and 100μM Casodex after 48h treatment on cell cycle kinetics and apoptosis were evaluated by flow cytometry. DNA content was detected using propidium iodide staining (B) and DNA fragmentation by analysis of Apo-BrdU incorporation (C). Results are representative of 3 independent experiments.

treatment of prostate cancer, and have investigate the molecular mechanisms which lead to cell cycle arrest and induction of apoptosis in prostate cancer cells.

Analysis of LNCaP cells treated with Casodex demonstrates a time and dose dependent decrease in cell number with statistically significant reductions in growth at 48h at doses of 50μM and greater (Figure 4A). Treatment with 50μM Casodex induces G_1 arrest with a concomitant decrease in both S and G_2 phase cell percentages (Figure 4B), but minimal apoptosis. Treatment with 100μM Casodex induces substantial apoptosis as monitored by Apo-BrDU staining and flow cytometry. (Figure 4C). The PC-346C cell line demonstrates asimilar time and dose dependent decreases in cell number but are slightly more sensitive to lower doses of Casodex (Figure 5A). Cell cycle analysis of PC-346C cells treated with 50μM Casodex shows a significant increase in the G_1 population accompanied by a decrease in the proportion of cells in S phase (Figure 5B) and a small population of apoptotic cells. Treatment with 100μM Casodex induces a significant increase in the proportion of cells undergoing apoptosis (22%) compared to control cells (Figure 5C). These data indicate that both LNCaP and PC-346C cells display similar sensitivity and response to treatment with Casodex, and that the threshold concentration of Casodex required to induce cell death in these androgen-dependent AR+ cell lines is between 50 and 100μM.

Gene expression in PC-346C cells is significantly altered following treatment with Casodex

To determine the effects of Casodex on gene expression, three independent sets of samples of PC-346C and four of LNCaP cells, consisting of vehicle control and 50μM Casodex treated cells were analyzed using the Nimblegen complete human gene array. The microarray analysis software GeneSpring 7.2 (Silicon Genetics) and Ingenuity pathway analysis software was used for detailed comparative analysis. Casodex treatment altered expression of 1325 genes by 1.8-fold or more in comparison to control. Following statistical analysis using ANOVA coupled with the Benjamani-Hochberg Multiple Testing Correction (MTC) ($p<0.05$) and elimination of genes with unknown functionality, the gene list was further reduced to 304 genes (Figure 6). Similar statistical analysis revealed 245 genes to be differentially regulated in Casodex treated LNCaP cells. Unexpectedly, the gene lists were significantly disparate, as greater than 70% of the genes populating the gene lists were uniquely regulated in the two cells lines. To determine additional genes which may be important in Casodex mediated growth arrest and apoptosis, the resultant gene lists were analyzed using Gene Ontology (GO) categorization available within GeneSpring. Of the Casodex regulated genes, 39 were cell cycle and death genes commonly regulated by both cell lines with an additional 42 and 47 specific to PC-346C and LNCaP cells, respectively (Figure 7). Although more than 50% of the genes are uniquely regulated in each cell line most of these were found to be associated with metabolic functions. We have annotated the complete lists of genes that are regulated by Casodex in LNCaP and PC-346C cells (Appendix 1 and 2) and in common between these cell lines (appendix 3 and 4). We have validated and significantly extended the gene array data using Real Time PCR to analyze both the time course and dose response of these changes in RNA levels using Rel-Time PCR (RT-PCR). To date we have analyzed 64 of the 120+ genes that are upregulated after treatment with Casodex in one cell line or the other, or in both cell lines. These data are tabulated in Tables 1 and 2.

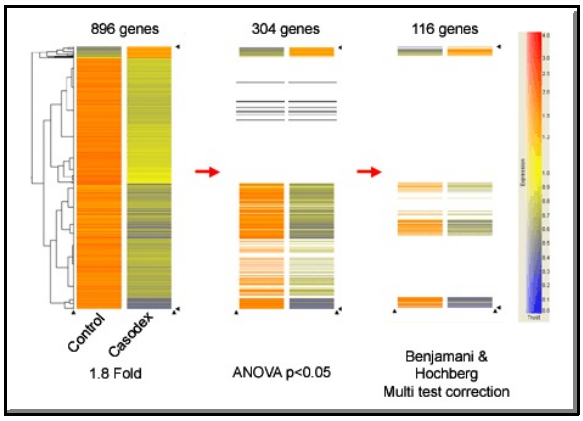


Figure 6: Gene array analysis of effects of Casodex on PC 346C cells

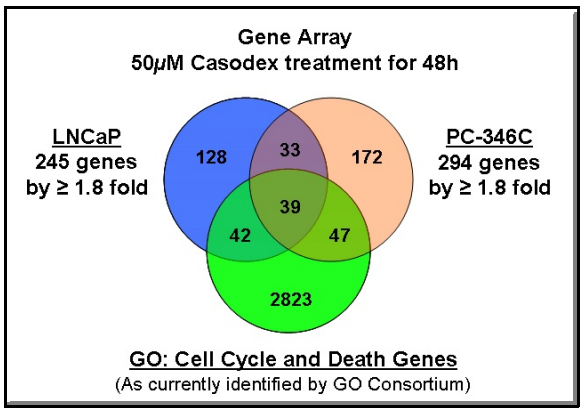


Figure 7: Venn Diagram showing overlap in genes up regulated by Casodex in LNCaP and PC-346C cells.

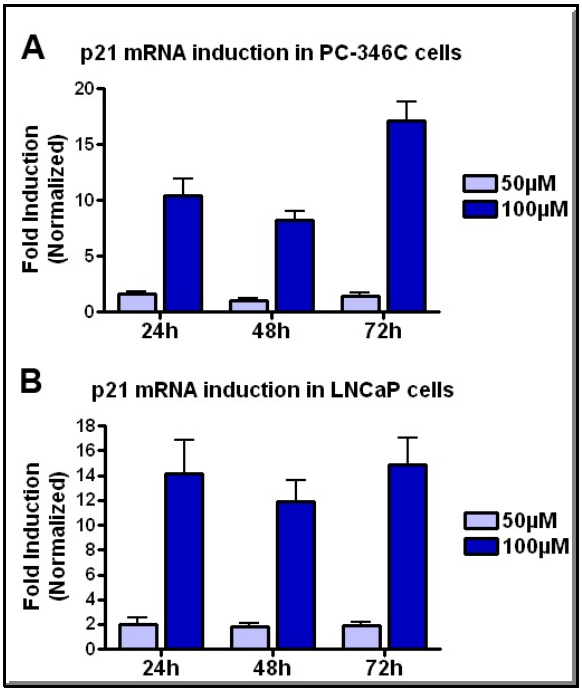


Figure 8 - Real-Time PCR analysis of p21 mRNA expression. Cells were treated for 24-72h with 0, 50 and 100µM Casodex. Harvested RNA was reverse-transcribed to cDNA and used for Real-time PCR analysis. Results indicate relative p21 mRNA expression levels in PC-346C (A) and LNCaP (B) cells in comparison to control, normalized against GAPDH.

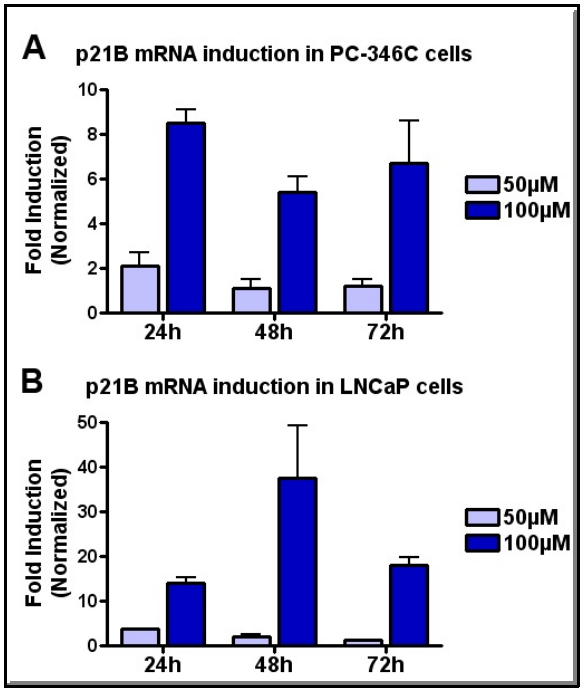


Figure 9 - Real-Time PCR analysis of p21B expression. Cells were treated for 24-72h with 0, 50 and 100µM Casodex. Harvested RNA was transcribed to cDNA and used for Real-time PCR analysis. Results indicate relative expression of p21B mRNA in PC-346C (A) and LNCaP (B) cells, which may transcribe a pro-apoptotic protein product. Results are normalized against GAPDH

Gene array reveals that while Casodex induces cell cycle arrest and apoptosis in both LNCaP and PC-346C and the drug induces many of the same genes in the two cell lines , there are also a number of genes that are uniquely regulated in each cell line . Using RT-PCR we have characterized the dose and time dependent effects of Casodex on approximately 60 of the responsive transcripts in the two cell lines (Summarized in Tables 1 and 2). Focusing on two representative transcripts- p21 (the cyclin dependent kinase inhibitor that induces G1 cell cycle arrest) and p21B (a newly discovered transcript related to p21 that initiates apoptosis),is shown in Figures 8 and 9. These data demonstrate that the induction of both of these genes is higly dependent on the dosage of Casodex and offers a molecular explanation for the observation of cell cycle arrest and apoptosis seen in Figures 4 and 5. *In silico* analysis of these data sets using proprietary Ingenuity Pathway Analysis software suggests that the sensitivity to Casodex may be mediated through the interaction between AR mediated signaling and p53 mediated transcriptional activation, an hypothesis we are currently investigating.

Taken together these data suggest that, in the context of a monotherapy, Casodex is likely to induce a significantly more robust regression of the localized primary tumors at doses of 150 mg/day or even 300mg/day trather than the lower doses of 50 mg/day that have been used in the past. Thus these studies may directly impact the treatment of prostate cancer in patients opting for hormone therapy.

Key Research Accomplishments

- Characterization of cellular pathways involved in induction of apoptosis after anti-androgen therapy in PC-3465C^{RFP} cells in vitro, with particular emphasis on the role of the mitochondria (documented in Lee et al., 2003 and Zhan et al., 2002)

- Publication of two review papers germane to this project, both of which reference the central hypothesis being tested in the experiments outlined in this report (Lee and Tenniswood 2004a, 2004b).

- Demonstration that invasive sublines of LNCaP cells are not highly metastatic in vivo, (probably due to the high levels of adrenal steroid, DHEA, in the rodent host).
- Establishment and refinement of new model of androgen dependent anti-androgen responsive localized prostate cancer

- Demonstration that treatment of orthotopic tumors derived from PC-346C^{RFP} cells induce apoptosis in response to Casodex

- Demonstration that Casodex treatment can also induce metastatic progression in the PC-346C^{RFP} cells, providing support for the suggestion that the LNCaP cell line and its derivatives may not be ideal model cell lines for orthotopic studies, and providing a possible explanation for the failure of the invasive LNCaP cells to metastasize.

- Development of a robust methodology for the isolation of RFP tagged cells from orthotopic tumors (primary and metastatic) that can be used for Gene array analysis and Western analysis.

- Microcroarray identification of < 1.8 fold changes in genes involved in mitosis, apoptosis or metastasis.
-
- Real Time PCR quantitation of the dose dependent and time dependent changes in gene expression

Reportable Outcomes

We have created a number of novel cell lines including:

- PC346C^{RFP}
- LNCaP^{RFP}
- PC346C^{GFP}
- DU-145^{RFP}
- DU-145^{GFP}

- We have extensive gene array data that we are planning to place on our website so that other investigators can access the raw data.

- RT-PCR data will be included in the upcoming manuscript(s) outlined below as Supplemental Data so that it will also be accessiblt to other investigators

This award has produced 6 manuscripts that have been published, and a further two manuscripts that are in the final stages of preparation which acknowledge the support of DAMD17-01-1-0114:

Zhan P., Lee, E.C.Y., Packman, K. and Tenniswood, M. (2002) Induction of Invasive Phenotype by Casodex in hormone sensitive Prostate Cancer Cells. *Journal of Steroid Biochemistry and Molecular Biology* 83: 101-111.

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TABLE 1: Dose Response and Time Course Analysis of Gene Expression in PC-346C cells treated with Casodex

Gene		24h	Error (SD)	48h	Error (SD)	72h	Error (SD)
CDC20	50uM	**-1.3**	0.2	**-11.3**	2.6	**-2.7**	0.4
	100uM	**1.0**	0.1	**-11.3**	0.9	**-34.7**	9.3
CCND1	50uM	**-1.4**	0.2	**-1.1**	0.1	**-1.4**	0.2
	100uM	**-1.2**	0.1	**-1.3**	0.1	**-1.2**	0.1
CCNB1	50uM	**-1.1**	0.1	**-7.4**	2.2	**-3.1**	0.6
	100uM	**-1.9**	0.1	**-8.3**	0.9	**-19.3**	3.6
ATF3	50uM	**3.0**	0.6	**2.0**	0.4	**1.6**	0.4
	100uM	**28.8**	3.8	**27.0**	3.6	**25.7**	5.5
CDC2	50uM	**-1.8**	0.2	**-5.0**	1.6	**-2.6**	0.2
	100uM	**-2.3**	0.2	**-16.4**	1.7	**-35.1**	2.8
E2F	50uM	**-2.6**	0.1	**-5.3**	1.1	**-2.0**	0.2
	100uM	**1.1**	0.2	**-7.3**	0.8	**-21.3**	2.2
AR	50uM	**1.2**	0.1	**1.2**	0.2	**1.8**	0.2
	100uM	**-1.4**	0.3	**-1.2**	0.1	**1.0**	0.1
CDC25A	50uM	**-2.5**	0.2	**-3.7**	0.6	**-2.1**	0.2
	100uM	**-1.6**	0.2	**-4.9**	0.6	**-6.6**	0.7
VEGF	50uM	**2.0**	0.3	**1.6**	0.2	**1.6**	0.2
	100uM	**7.4**	0.3	**7.3**	0.6	**9.2**	1.5
BTG	50uM	**-2.3**	0.6	**-1.7**	0.1	**-1.7**	0.1
	100uM	**1.3**	0.2	**-2.1**	0.2	**3.8**	0.3
EGF	50uM	**2.6**	0.3	**3.2**	0.4	**3.5**	0.4
	100uM	**3.5**	0.7	**5.3**	0.6	**7.9**	0.9
SERPIN B	50uM	**2.3**	0.2	**1.7**	0.5	**1.2**	0.4
	100uM	**4.6**	0.3	**1.8**	0.5	**2.2**	0.6
p21all	50uM	**1.6**	0.2	**1.0**	0.2	**1.4**	0.2
	100uM	**10.4**	1.5	**8.2**	0.8	**17.1**	1.7
p21B s2	50uM	**2.1**	0.6	**-1.6**	0.6	**1.2**	0.3
	100uM	**6.9**	1.4	**4.4**	0.9	**5.8**	1.4
CCNB2	50uM	**1.1**	0.2	**-6.0**	1.4	**-2.2**	0.1
	100uM	**1.5**	0.2	**-5.3**	0.4	**-17.8**	2.9
CCND3	50uM	**-1.5**	0.2	**-1.6**	0.1	**-1.5**	0.2
	100uM	**1.1**	0.1	**-1.9**	0.2	**-1.6**	0.2
PCNA	50uM	**-1.9**	0.2	**-3.2**	0.3	**-1.7**	0.2
	100uM	**-1.3**	0.1	**-2.6**	0.3	**-3.1**	0.4
MCM7	50uM	**-2.1**	0.2	**-3.6**	0.5	**-1.8**	0.2
	100uM	**1.2**	0.2	**-2.4**	0.2	**-2.2**	0.2
Survivin	50uM	**-1.4**	0.1	**-9.3**	1.6	**-2.4**	0.3
	100uM	**-1.2**	0.1	**-16.9**	2.2	**-64.0**	16.6
p8	50uM	**2.4**	0.1	**4.8**	0.4	**3.2**	0.3
	100uM	**7.7**	0.4	**15.5**	1.3	**11.0**	0.4
PLK1	50uM	**-1.0**	0.1	**-11.1**	3.2	**-2.8**	0.3
	100uM	**-1.3**	0.3	**-31.3**	3.0	**-97.4**	5.7
CCNE1	50uM	**-2.5**	0.3	**-1.9**	0.3	**-1.3**	0.2
	100uM	**1.5**	0.3	**-1.3**	0.2	**-1.9**	0.2
p53	50uM	**1.8**	0.3	**1.5**	0.3	**1.4**	0.2
	100uM	**6.4**	0.9	**4.8**	1.1	**4.7**	0.5
CCNA2	50uM	**-1.2**	0.1	**-8.5**	2.1	**-1.9**	0.4
	100uM	**-2.4**	0.3	**-22.3**	1.7	**-97.2**	19.5
CCNH	50uM	**1.2**	0.2	**1.2**	0.1	**1.2**	0.2
	100uM	**2.8**	0.5	**2.4**	0.1	**1.5**	0.3
CDK2	50uM	**-1.7**	0.2	**-2.6**	0.2	**-1.2**	0.2
	100uM	**1.1**	0.1	**-2.2**	0.2	**-1.4**	0.1
CDK4	50uM	**1.1**	0.2	**-1.2**	0.1	**1.1**	0.1
	100uM	**2.1**	0.3	**1.2**	0.2	**1.6**	0.1
p27	50uM	**1.7**	0.2	**2.5**	0.4	**1.6**	0.3
	100uM	**2.5**	0.1	**2.3**	0.4	**3.5**	0.4

CDC45A	50uM	**-2.3**	0.3	**-6.7**	1.3	**-1.6**	0.1
	100uM	**1.1**	0.1	**-12.3**	1.5	**-66.9**	3.0
DNMT1	50uM	**-2.0**	0.8	**-5.0**	0.9	**-2.5**	0.5
	100uM	**1.0**	0.4	**-4.3**	1.0	**-3.0**	0.7
CEBPB	50uM	**3.2**	0.2	**3.2**	0.3	**2.6**	0.3
	100uM	**7.8**	0.6	**12.7**	0.9	**14.4**	0.8
p18	50uM	**-1.6**	0.0	**-3.1**	0.5	**-1.7**	0.2
	100uM	**-2.3**	0.2	**-6.1**	0.6	**-4.8**	0.3
IGF1	50uM	**-3.2**	0.2	**-1.9**	0.5	**-2.3**	0.4
	100uM	**-2.0**	0.4	**-19.9**	4.0	**-3.0**	0.5
IGF	50uM	**-3.2**	0.2	**-1.9**	0.5	**-2.3**	0.4
	100uM	**-2.0**	0.4	**-19.9**	4.0	**-3.0**	0.5
IGFR1	50uM	**-1.1**	0.1	**1.3**	0.2	**-1.1**	0.2
	100uM	**1.2**	0.2	**1.3**	0.1	**1.2**	0.2
IGFR	50uM	**-1.3**	0.2	**1.2**	0.3	**-1.0**	0.1
	100uM	**1.2**	0.1	**1.5**	0.3	**1.2**	0.2
ACK1	50uM	**-1.9**	0.1	**-2.1**	0.3	**-1.7**	0.3
	100uM	**1.6**	0.1	**-1.9**	0.2	**-1.5**	0.2
KLK2	50uM	**-3.7**	0.4	**-2.6**	0.5	**-2.0**	0.2
	100uM	**-14.0**	2.9	**-76.9**	19.8	**-58.0**	8.9
MDM2	50uM	**1.1**	0.2	**-1.1**	0.3	**1.2**	0.2
	100uM	**1.7**	0.2	**-1.0**	0.3	**3.7**	0.4
MYC	50uM	**-1.2**	0.1	**1.2**	0.1	**1.3**	0.4
	100uM	**-2.7**	0.4	**-2.8**	0.2	**-1.6**	0.6
POLA2	50uM	**-2.1**	0.1	**-3.7**	0.4	**-1.7**	0.2
	100uM	**1.5**	0.2	**-3.0**	0.3	**-4.4**	0.4
RAD21	50uM	**1.1**	0.1	**-1.3**	0.2	**1.2**	0.3
	100uM	**1.7**	0.2	**1.4**	0.2	**1.4**	0.4
RB1	50uM	**1.0**	0.1	**1.0**	0.2	**1.1**	0.1
	100uM	**2.1**	0.1	**1.9**	0.2	**2.0**	0.2
SP1	50uM	**1.1**	0.2	**1.2**	0.3	**1.1**	0.2
	100uM	**2.6**	1.5	**1.9**	0.3	**2.1**	0.4
BNIP3L	50uM	**1.1**	0.1	**1.3**	0.0	**1.3**	0.1
	100uM	**1.2**	0.3	**2.9**	0.3	**2.7**	0.4
TP53I3	50uM	**1.4**	0.3	**-1.1**	0.2	**-1.2**	0.2
	100uM	**1.9**	0.1	**2.7**	0.6	**2.1**	0.2
NFKB1	50uM	**1.1**	0.1	**1.2**	0.1	**1.1**	0.1
	100uM	**1.7**	0.1	**1.1**	0.1	**1.5**	0.2
CLU	50uM	**-1.4**	0.0	**-1.3**	0.1	**-1.3**	0.1
	100uM	**-1.0**	0.1	**1.4**	0.1	**1.3**	0.1
WEE1	50uM	**1.1**	0.1	**-2.3**	0.5	**-1.1**	0.2
	100uM	**1.1**	0.3	**-1.8**	0.3	**-1.2**	0.3
AKT1	50uM	**-1.0**	0.1	**1.1**	0.1	**1.1**	0.2
	100uM	**-1.3**	0.2	**-1.2**	0.1	**1.1**	0.2
ATF4	50uM	**1.5**	0.3	**2.0**	0.2	**1.7**	0.2
	100uM	**2.5**	0.4	**2.3**	0.3	**4.8**	0.6
BNIP3	50uM	**1.1**	0.3	**1.1**	0.1	**-1.1**	0.1
	100uM	**1.4**	0.3	**-1.3**	0.1	**1.7**	0.1
DDIT3	50uM	**4.3**	0.4	**3.2**	0.8	**2.5**	0.6
	100uM	**13.3**	1.2	**25.9**	5.6	**25.1**	3.8
CDKN2B	50uM	**2.1**	0.3	**1.7**	0.5	**1.9**	0.3
	100uM	**2.9**	0.5	**8.3**	2.6	**14.3**	3.2
BIRC4	50uM	**1.4**	0.1	**1.4**	0.2	**1.5**	0.2
	100uM	**3.7**	0.3	**4.3**	0.4	**4.2**	0.5

TABLE 2: Dose Response and Time Course Analysis of Gene Expression in LNCaP cells treated with Casodex

Gene		24h	Error (SD)	48h	Error (SD)	72h	Error (SD)
CDC20	50uM	-1.3	0.2	-5.2	0.7	-3.0	0.5
	100uM	-2.9	0.4	-432.2	40.2	-59.8	7.4
CCND1	50uM	-1.3	0.2	-1.1	0.1	-1.0	0.2
	100uM	-5.3	0.9	-13.2	1.8	-3.6	0.6
CCNB1	50uM	1.1	0.2	-4.3	0.5	-1.8	0.4
	100uM	-2.4	0.4	-31.4	2.9	-16.5	2.2
ATF3	50uM	1.9	0.4	1.7	0.2	1.7	0.2
	100uM	26.5	3.1	18.3	1.8	23.7	4.8
CDC2	50uM	-1.2	0.4	-3.1	0.4	-2.5	0.4
	100uM	-2.9	0.8	-61.3	6.6	-26.5	2.3
E2F	50uM	-1.5	0.3	-2.5	0.5	-2.2	0.4
	100uM	-1.1	0.2	-23.6	5.1	-7.6	1.2
AR	50uM	-1.1	0.3	1.3	0.1	1.3	0.1
	100uM	-4.5	0.9	-2.5	0.2	-2.0	0.2
CDC25A	50uM	-1.1	0.2	-2.0	0.2	-1.8	0.1
	100uM	-1.4	0.2	-7.6	0.3	-3.3	0.3
VEGF	50uM	2.0	0.3	2.6	0.4	1.8	0.2
	100uM	6.3	0.9	12.6	1.5	15.1	2.2
BTG	50uM	-2.3	0.6	-1.7	0.1	-1.7	0.1
	100uM	1.3	0.2	-2.1	0.2	3.8	0.3
EGF	50uM	1.8	0.3	2.1	0.2	1.3	0.2
	100uM	3.5	0.2	4.6	0.2	8.9	1.0
SERPIN B	50uM	3.8	0.9	2.0	1.4	3.1	0.4
	100uM	11.3	7.7	2.2	0.5	5.8	1.1
p21all	50uM	2.0	0.5	1.8	0.3	1.9	0.3
	100uM	14.1	2.7	11.9	1.7	14.9	2.1
p21B s2	50uM	2.7	0.3	1.5	0.4	1.1	0.2
	100uM	13.3	1.7	38.8	11.1	18.9	3.6
CCNB2	50uM	-1.3	0.3	-5.4	0.7	-2.6	0.5
	100uM	-2.3	0.4	-51.3	4.3	-57.0	8.6
CCND3	50uM	-1.1	0.1	-1.3	0.1	-1.2	0.2
	100uM	1.1	0.1	-1.9	0.2	-1.6	0.2
PCNA	50uM	-1.2	0.2	-2.5	0.4	-1.7	0.2
	100uM	-1.8	0.3	-10.7	1.4	-2.1	0.2
MCM7	50uM	-1.2	0.2	-2.9	0.1	-2.1	0.4
	100uM	-2.2	0.3	-10.2	0.5	-6.0	0.5
Survivin	50uM	-1.8	0.1	-4.6	0.8	-2.1	0.3
	100uM	-3.5	0.3	-258.0	30.4	-78.6	12.0
p8	50uM	1.2	0.1	1.6	0.1	1.5	0.2
	100uM	2.5	0.2	-2.2	0.1	4.5	0.7
PLK1	50uM	1.1	0.1	-5.0	0.7	-3.6	0.9
	100uM	-2.8	0.2	-133.4	13.7	-236.7	42.9
CCNE1	50uM	-1.1	0.1	-1.5	0.1	-1.5	0.2
	100uM	-1.3	0.1	-2.8	0.0	-2.6	0.1
p53	50uM	2.1	0.1	1.5	0.2	1.0	0.3
	100uM	2.7	0.2	1.1	0.2	1.4	0.2
ACK1	50uM	2.0	0.3	1.2	0.1	-1.1	0.1
	100uM	1.7	0.2	6.8	0.4	1.1	0.1
CCNA2	50uM	-1.4	0.3	-5.8	1.2	-3.1	0.6
	100uM	-5.8	1.1	-176.8	41.8	-82.5	23.5
CCNH	50uM	1.7	0.4	1.1	0.0	1.3	0.2
	100uM	1.2	0.3	-1.4	0.1	1.7	0.3
CDK2	50uM	-1.3	0.1	-2.2	0.1	-1.8	0.1
	100uM	-1.9	0.2	-6.5	0.3	-3.8	0.1
CDK4	50uM	-1.1	0.1	-1.5	0.0	-1.4	0.1
	100uM	-1.0	0.0	-3.6	0.1	1.1	0.2
p27	50uM	1.1	0.2	1.2	0.2	1.4	0.1
	100uM	2.1	0.2	1.8	0.2	3.4	0.4
CDC45A	50uM	-1.1	0.3	-3.5	0.2	-2.0	0.3
	100uM	-1.3	0.3	-82.1	15.2	-131.2	36.8
DNMT1	50uM	-1.5	0.2	-1.7	0.2	-1.9	0.3
	100uM	-1.1	0.3	-2.4	0.4	-2.2	0.2
CEBPB	50uM	1.1	0.1	2.2	0.4	1.7	0.2
	100uM	3.9	0.3	3.3	0.2	7.3	0.7
p18	50uM	-1.3	0.2	-3.1	0.5	-2.1	0.3
	100uM	-2.0	0.2	-51.1	5.7	-9.3	0.9
IGF1	50uM	-2.0	0.5	-6.8	1.2	-3.9	0.9
	100uM	-4.8	1.1	-15.1	1.3	-2.4	0.6
IGF	50uM	-1.6	0.5	-6.1	0.6	-1.9	0.2
	100uM	-3.0	0.6	-13.4	2.2	-2.5	0.2
IGFR1	50uM	-3.1	0.6	-7.1	1.8	-4.0	0.8
	100uM	-9.1	1.7	-10.8	1.9	-8.3	1.3
IGFR	50uM	-2.6	0.3	-3.7	1.0	-3.1	0.3
	100uM	-8.9	0.9	-6.0	0.6	-6.9	0.8

ACK1	50uM	**1.9**	0.4	**1.0**	0.5	**1.0**	0.1
	100uM	**1.6**	0.2	**8.8**	1.3	**1.2**	0.1
KLK2	50uM	**-6.6**	0.5	**-8.4**	1.7	**-9.6**	1.9
	100uM	**-21.2**	3.0	**-848.0**	148.4	**-211.8**	29.7
MDM2	50uM	**1.1**	0.2	**-1.1**	0.3	**1.2**	0.2
	100uM	**1.7**	0.2	**-1.0**	0.3	**3.7**	0.4
MYC	50uM	**-1.2**	0.2	**-1.4**	0.1	**-1.3**	0.1
	100uM	**-3.7**	0.4	**-33.4**	2.6	**-5.3**	0.6
POLA2	50uM	**1.1**	0.2	**-2.0**	0.1	**-1.6**	0.2
	100uM	**-1.5**	0.3	**-10.3**	0.4	**-3.3**	0.1
RAD21	50uM	**-1.2**	0.1	**-1.8**	0.2	**-1.4**	0.1
	100uM	**-1.2**	0.2	**-2.1**	0.2	**-1.1**	0.1
RB1	50uM	**-1.1**	0.1	**-1.4**	0.1	**-1.2**	0.1
	100uM	**1.5**	0.1	**1.1**	0.0	**1.6**	0.2
SP1	50uM	**1.5**	0.1	**1.0**	0.1	**-1.4**	0.1
	100uM	**2.1**	0.4	**1.3**	0.1	**1.4**	0.1
BNIP3L	50uM	**1.1**	0.1	**1.9**	0.2	**1.2**	0.2
	100uM	**1.4**	0.1	**-6.6**	1.0	**3.5**	0.5
TP53I3	50uM	**2.5**	0.5	**3.2**	0.4	**2.0**	0.3
	100uM	**12.3**	1.9	**3.4**	0.2	**6.9**	0.7
NFKB1	50uM	**1.2**	0.1	**1.3**	0.1	**1.2**	0.1
	100uM	**-1.5**	0.2	**-1.2**	0.1	**1.7**	0.1
CLU	50uM	**1.2**	0.2	**3.0**	0.4	**3.5**	0.5
	100uM	**1.1**	0.2	**2.2**	0.2	**8.6**	1.3
WEE1	50uM	**1.0**	0.2	**-2.0**	0.1	**-1.6**	0.2
	100uM	**-1.2**	0.3	**-2.6**	0.3	**1.1**	0.2
AKT1	50uM	**1.0**	0.1	**-1.1**	0.2	**1.0**	0.2
	100uM	**-1.5**	0.0	**-1.2**	0.2	**1.1**	0.1
ATF4	50uM	**1.5**	0.3	**2.0**	0.2	**1.7**	0.2
	100uM	**2.5**	0.4	**2.3**	0.3	**4.8**	0.6
BNIP3	50uM	**1.1**	0.3	**1.1**	0.1	**-1.1**	0.1
	100uM	**1.4**	0.3	**-1.3**	0.1	**1.7**	0.1

APPENDIX 1: Summary of Uniquely Regulated Genes in LNCaP cells Passing the 1.8 Fold Cut-off After Benjamani-Hochberg MTC

GenBank ID	Fold Change	Common Name	Description
NM_182513	4.695	Spc24; FLJ90806	spindle pole body component 24 homolog (S. cerevisiae)
NM_001827	4.109	CKSHS2	CDC28 protein kinase regulatory subunit 2
NM_001034	3.306	R2; RR2M	ribonucleotide reductase M2 polypeptide
NM_003817	3.286	EAPI; GP-83	ADAM metallopeptidase domain 7
NM_018455	3.173	BM039	uncharacterized bone marrow protein BM039
NM_015261	3.022	hCAP-D3; KIAA0056; MGC104671	KIAA0056 protein
NM_005914	2.96	CDC21; CDC54; hCdc21; MGC33310; P1-CDC21	MCM4 minichromosome maintenance deficient 4 (S. cerevisiae)
NM_017975	2.875	KNTC1AP; hZwilch; FLJ10036; MGC111034	Zwilch, kinetochore associated, homolog (Drosophila)
NM_012484	2.702	IHABP; RHAMM; MGC119494; MGC119495	hyaluronan-mediated motility receptor (RHAMM)
BC036704	2.641	SCS; ACS3; BPES2; BPES3; TWIST	twist homolog 1 (acrocephalosyndactyly 3; Saethre-Chotzen syndrome) (Drosophila)
NM_016343	2.61	CENF; PRO1779	centromere protein F, 350/400ka (mitosin)
BC066948	2.581	ZNF286	Peroxisome proliferative activated receptor, alpha-like
NM_015895	2.559	Gem; RP3-369A17.3	geminin, DNA replication inhibitor
NM_005030	2.525	PLK; STPK13	polo-like kinase 1 (Drosophila)
BC062456	2.497	CANP	cancer-associated nucleoprotein
BC033086	2.467	SC1; SC1-1	transcription factor 19 (SC1)
NM_030919	2.45	FAM83D; dJ616B8.3	chromosome 20 open reading frame 129
AF053306	2.439	SSK1; BUBR1; Bub1A; MAD3L; hBUBR1; BUB1beta	BUB1 budding uninhibited by benzimidazoles 1 homolog beta (yeast)
BC004236	2.409	E2-EPF	ubiquitin-conjugating enzyme E2S
AF318374	2.407	TMPRSS2	Transmembrane protease, serine 2
NM_024094	2.401	DCC1; MGC5528	defective in sister chromatid cohesion homolog 1 (S. cerevisiae)
BX248255	2.392	DLG1; HURP; KIAA0008	discs, large homolog 7 (Drosophila)
AY223851	2.387	ADAM33	ADAM metallopeptidase domain 33
NM_033102	2.369	PRST; IPCA-6; PCANAP6	solute carrier family 45, member 3
AF229835	2.365	LYAR; FLJ20425	hypothetical protein FLJ20425
NM_012145	2.359	CDC8; TMPK; TYMK	deoxythymidylate kinase (thymidylate kinase)
L19183	2.348	MAC30	hypothetical protein MAC30
NM_032117	2.333	GAJ; MND1	GAJ protein
NM_014791	2.307	HPK38; KIAA0175	maternal embryonic leucine zipper kinase
BC010105	2.281	FLB7527; MGC2297; PRO1999; FLJ31599; FLJ35510; MGC19722; MGC20372; DKFZp547F162	nuclear autoantigenic sperm protein (histone-binding)
NM_002915	2.258	RFC38; MGC5276	replication factor C (activator 1) 3, 38kDa
AL137506	2.255	FLJ23563	ELOVL family member 7, elongation of long chain fatty acids (yeast)
AB041267	2.241	K19; CK19; K1CS; MGC15366	keratin 19
BC062761	2.232	V2; TCRGV9; T-cell receptor, gamma, variable region V9	T cell receptor gamma variable 9
NM_182908	2.23	HEP27	dehydrogenase/reductase (SDR family) member 2
NM_004900	2.205	ARP4; ARCD3; PHRBNL; APOBEC1L; FLJ21201; DJ742C19.2	apolipoprotein B mRNA editing enzyme, catalytic polypeptide-like 3B
NM_005410	2.193	SeP; SELP	selenoprotein P, plasma, 1
NM_175834	2.177	KRT6L	keratin 6L
BC035819	2.174	CESC1	synaptonemal complex central element protein 2
NM_001003799	2.174	TARP; TCRGC1	TCR gamma alternate reading frame protein
NM_003115	2.168	AgX; AGX1; SPAG2	UDP-N-acteylglucosamine pyrophosphorylase 1
NM_004488	2.153	CD42d	glycoprotein V (platelet)
AJ549095	2.146	N/A	short variant; Homo sapiens t(7; 16)(q33; p11) translocation breakpoint mRNAmaeric BBF2H7/FUS protein,
NM_014865	2.132	CNAP1; KIAA0159	chromosome condensation-related SMC-associated protein 1
NM_182802	2.126	MGC4816; MGC12866; C20orf154; MGC119522; MGC119523; dJ967N21.5	MCM8 minichromosome maintenance deficient 8 (S. cerevisiae)
NM_025080	2.078	ALP; ALP1; FLJ22316	asparaginase like 1
Y16676	2.064	GTBP; HSAP; HNPCC5	mutS homolog 6 (E. coli)
NM_001798	2.053	p33(CDK2)	cyclin-dependent kinase 2
NM_002916	2.042	A1; RFC37; MGC27291	replication factor C (activator 1) 4, 37kDa
NM_002764	2.023	PRSI; PRS I; KIAA0967	phosphoribosyl pyrophosphate synthetase 1
NM_006287	2.012	EPI; LACI	tissue factor pathway inhibitor (lipoprotein-associated coagulation inhibitor)
AF237700	1.999	RGP2; NUP358; RANBP2L2	RANBP2-like and GRIP domain containing 2
NM_021637	1.98	FLJ14084	transmembrane protein 35
NM_001254	1.968	CDC18L; HsCDC6; HsCDC18	CDC6 cell division cycle 6 homolog (S. cerevisiae)
NM_022731	1.961	JC7; NUCKS; FLJ21480	nuclear casein kinase and cyclin-dependent kinase substrate 1
NM_000742	1.949	CHRNA2	cholinergic receptor, nicotinic, alpha polypeptide 2 (neuronal)
AF070418	1.945	HEED; WAIT1	embryonic ectoderm development
L29138	1.933	myr1	myosin IB
NM_023037	1.93	13CDNA73; CG003; 214K23.2; C13orf14; bA207N4.2	hypothetical protein CG003
BC001866	1.926	RFC36; MGC1155	replication factor C (activator 1) 5, 36.5kDa
NM_013290	1.923	TBPIP; GT198	TBP-1 interacting protein
NM_017906	1.92	PIP1; hPIP1; FLJ20624; bA421M1.5; RP11-421M1.5	PAK1 interacting protein 1
NM_199249	1.914	MGC13170	multidrug resistance-related protein
AY211919	1.914	NY-SAR-48; MGC20533	sarcoma antigen NY-SAR-48
NM_013233	1.91	DCHT; SPAK	serine threonine kinase 39 (STE20/SPS1 homolog, yeast)
NM_130898	1.893	JAL; hJAL; ATCE1; CREB3; CREB4; AIBZIP	cAMP responsive element binding protein 3-like 4
BC015586	1.882	LAMB2; MGC87297	laminin, gamma 1 (formerly LAMB2)
U87954	1.88	EBP1; p38-2G4	proliferation-associated 2G4, 38kDa
NM_024745	1.879	FLJ22009; MGC26900	SHC SH2-domain binding protein 1
BC021299	1.878	PDEF; bA375E1.3; RP11-375E1__A.3	SAM pointed domain containing ets transcription factor
AF116690	1.872	ACS3; FACL3; PRO2194	acyl-CoA synthetase long-chain family member 3
AK125506	1.865	KIAA0870	DENN/MADD domain containing 3
BC025025	1.864	GH	gamma-glutamyl hydrolase (conjugase, folylpolygammaglutamyl hydrolase)
NM_015238	1.863	KIBRA; KIAA0869	KIBRA protein
AF039575	1.86	P37; AUF1; AUF1A; hnRNPD0	heterogeneous nuclear ribonucleoprotein D (AU-rich element RNA binding protein 1, 37kDa)
NM_015161	1.858	AIP1; ARMER; ARL6IP1; KIAA0069	ADP-ribosylation factor-like 6 interacting protein
NM_014033	1.858	DKFZP586A0522; UbiE; AAM-B	DKFZP586A0522 protein
NM_001003800	1.852	KIAA0699; bA526D8.1	bicaudal D homolog 2 (Drosophila)
BC065745	1.847	DNAJA5	DnaJ homology subfamily A member 5
NM_012117	1.845	HP1; HP1-ALPHA; HP1Hs-alpha	chromobox homolog 5 (HP1 alpha homolog, Drosophila)
NM_005968	1.836	HTGR1; NAGR1; HNRNPM; HNRPM4; HNRNPM4; DKFZp547H118	heterogeneous nuclear ribonucleoprotein M
BC006550	1.834	RNMX; HNRPG; RBMXP1; RBMXRT	RNA binding motif protein, X-linked
NM_007317	1.83	KID; OBP; KNSL4; OBP-1; OBP-2	kinesin family member 22
AF053305	1.824	BUB1A; BUB1L; hBUB1	BUB1 budding uninhibited by benzimidazoles 1 homolog (yeast)
AL834350	1.824	B56G; MGC23064	protein phosphatase 2, regulatory subunit B (B56), gamma isoform
NM_178822	1.821	CMF608; FLJ25972	immunoglobulin superfamily, member 10

NM_003759	1.821	KNBC; NBC1; NBC2; pNBC; HNBC1; hhNMC; SLC4A5; DKFZp781H1314	solute carrier family 4, sodium bicarbonate cotransporter, member 4
AF161373	1.816	DPK; JIK; MAP3K18; DKFZp666H245	TAO kinase 3
AK000768	1.816	FLJ40851	Ca2+-dependent activator protein for secretion 2
NM_148957	1.813	TAJ; TROY; TRADE; TAJ-alpha	tumor necrosis factor receptor superfamily, member 19
BC030984	1.813	IGLC2	Immunoglobulin lambda joining 3
AK000113	1.81	SIAT7A; HSY11339; ST6GalNAcI	ST6 (alpha-N-acetyl-neuraminyl-2,3-beta-galactosyl-1,3)-N-acetylgalactosaminide alpha-2,6-sialyltransferase
NM_152463	1.807	MMS4L; FLJ31364	essential meiotic endonuclease 1 homolog 1 (S. pombe)
BC062532	1.807	M40; TUBB1; TUBB5; MGC16435; MGC117247; OK/SW-cl.56	tubulin, beta
BC011602	1.802	RTS; RECQ4	RecQ protein-like 4
NM_013277	1.802	ID-GAP; HsCYK-4; MgcRacGAP	Rac GTPase activating protein 1
NM_145001	0.553	YANK1; MGC22688	serine/threonine kinase 32A
NM_172373	0.552	ELF1	E74-like factor 1 (ets domain transcription factor)
NM_003944	0.552	LPSB; SP56; hSBP; hSP56; FLJ13813	selenium binding protein 1
NM_080654	0.551	L15; RAMA3; NY-REN-41	coiled-coil domain containing 34
U58146	0.55	CD130; GP130; CDw130; IL6R-beta; GP130-RAPS	interleukin 6 signal transducer (gp130, oncostatin M receptor)
BC017869	0.549	Fbx36; FLJ37592; FLJ41090	F-box protein 36
AY562998	0.549	N33; D8S1992; MGC13453	tumor suppressor candidate 3
AF161465	0.547	HSPC116	single-stranded DNA binding protein 2
NM_006214	0.546	RD; LN1; PAHX; LNAP1	phytanoyl-CoA hydroxylase
AF548389	0.546	UGT2B8	UDP glucuronosyltransferase 2 family, polypeptide B15
NM_016424	0.543	CROP; LUC7A; OA48-18	cisplatin resistance-associated overexpressed protein
BC007034	0.542	MT2	metallothionein 2A
AF034840	0.542	HB6; CD39L3; NTPDase-3	ectonucleoside triphosphate diphosphohydrolase 3
AF108756	0.541	FGF13	Fibroblast growth factor 13 isoform 1y1v (FGF13)
AL832329	0.541	p53RFP; KIAA0161; MGC71786; bA528A10.3	IBR domain containing 2
AJ506054	0.541	HLA-B	Major histocompatibility complex, class I, B
NM_177980	0.54	VR20	cadherin-like 26
AF049614	0.539	NRP; FIP2; HIP7; HYPL; GLC1E; TFIIIA-INTP	optineurin
BX641004	0.538	p54; dJ677H15.2; DKFZp686M13204	splicing factor, arginine/serine-rich 11
NM_181077	0.538	GM88	golgi autoantigen, golgin subfamily a, 8A
NM_000092	0.538	CA44	collagen, type IV, alpha 4
NM_018490	0.537	GPR48	leucine-rich repeat-containing G protein-coupled receptor 4
AK022900	0.535	hEndo; FLJ12838	mannosidase, endo-alpha
BC039461	0.534	DKFZP564A022	ring finger protein 170
AK095738	0.534	SMARCE1	SWI/SNF related, matrix associated, actin dependent regulator of chromatin, subfamily e, member 1
AK027867	0.532	VIA; SEMA; HT018; SEMAQ; SEMA6A1; KIAA1368; sema VIa	sema domain, transmembrane domain (TM), and cytoplasmic domain, (semaphorin) 6A
NM_033014	0.529	OIF; SLRR3A; DKFZP586P2421	osteoglycin (osteoinductive factor, mimecan)
BC001874	0.528	p60; p62; PDB3; ZIP3	sequestosome 1
AF155103	0.527	ANKRD13A; NY-REN-25	ankyrin repeat domain 13
AB002351	0.527	SYN; KIAA0353	desmuslin
NM_014007	0.526	ZNF-X; ZBTB22B	zinc finger protein 297B
NM_078487	0.522	P15; MTS2; TP15; INK4B	cyclin-dependent kinase inhibitor 2B (p15, inhibits CDK4)
AL834298	0.521	MAP1A/1BLC3	microtubule-associated protein 1 light chain 3 beta
NM_000574	0.52	CR; TC; CD55	decay accelerating factor for complement (CD55, Cromer blood group system)
NM_018557	0.52	LRPDIT; LRP-DIT	low density lipoprotein-related protein 1B (deleted in tumors)
NM_198569	0.516	DREG; VIGR; PS1TP2	G protein-coupled receptor 126
BC012947	0.515	CS1; CS-1; KRAP; SPAG13; KIAA1927; DKFZp779G0129	sperm specific antigen 2
NM_020987	0.515	ANKYRIN-G	ankyrin 3, node of Ranvier (ankyrin G)
AK127110	0.513	NIF3L1	NIF3 NGG1 interacting factor 3-like 1 (S. pombe)
AB002365	0.512	BMCC1; BNIPXL; A214N16.3; bA214N16.3	KIAA0367
NM_001167	0.511	API3; ILP1; MIHA; XIAP	baculoviral IAP repeat-containing 4
AB020634	0.506	NFATZ; OREBP; NF-AT5; NFATL1; TONEBP; KIAA0827	nuclear factor of activated T-cells 5, tonicity-responsive
NM_017905	0.506	C13orf11; FLJ20623	transmembrane and coiled-coil domains 3
X97261	0.505	MT1; MTF; MT1R; metallothionein 1R	metallothionein 1L
AJ583820	0.505	C10orf29; FLJ37318; bA137L10.3; bA137L10.4	ubiquitin specific peptidase 54
NM_138432	0.503	SDS-RS1	serine dehydratase-like
AB037794	0.503	AMSH-FP; AMSH-LP; ALMalpha; FLJ31524; KIAA1373; bA399O19.2	STAM binding protein-like 1
L47232	0.502	P21; CIP1; SDI1; WAF1; CAP20; CDKN1; MDA-6; p21CIP1	cyclin-dependent kinase inhibitor 1A (p21, Cip1)
NM_005949	0.496	MT1; MGC32732	metallothionein 1F (functional)
NM_003069	0.49	SWI2; SNF2L; SNF2L1; SNF2LB	SWI/SNF related, matrix associated, actin dependent regulator of chromatin, subfamily a, member 1
AY137774	0.489	4.1O; P410; EPB41L4O; MGC20553; RP11-439K3.2	FERM domain containing 3
NM_005311	0.489	RSS; IRBP; MEG1; GRB-IR; KIAA0207	growth factor receptor-bound protein 10
NM_002395	0.482	MES; HUMNDME	malic enzyme 1, NADP(+)-dependent, cytosolic
NM_005900	0.479	BSP1; JV41; JV4-1; MADH1; MADR1	SMAD, mothers against DPP homolog 1 (Drosophila)
AK094866	0.477	MGC126506	huntingtin interacting protein 1
NM_005611	0.473	Rb2; P130	retinoblastoma-like 2 (p130)
NM_020873	0.47	NLRR-1; KIAA1497	leucine rich repeat neuronal 1
NM_000598	0.467	IBP3; BP-53	insulin-like growth factor binding protein 3
NM_012397	0.466	HUR7; PI13; headpin; MGC126870	serpin peptidase inhibitor, clade B (ovalbumin), member 13
AB067489	0.46	FHOD2	formin-like 2
NM_018584	0.454	PRO1489; MGC22256; CaMKIINalpha; RP11-401M16.1	calcium/calmodulin-dependent protein kinase II inhibitor 1
NM_014959	0.443	DACAR; NDPP1; TUCAN; CARDINAL; KIAA0955	caspase recruitment domain family, member 8
AF409114	0.443	SIP; Teap; FLJ22139; p53DINP1; TP53DINP1; TP53INP1A; TP53INP1B; DKFZp434M1317	tumor protein p53 inducible nuclear protein 1
L20941	0.441	FTH; PLIF; FTHL6; PIG15; MGC104426	ferritin, heavy polypeptide 1
U46689	0.437	SLS; FALDH; ALDH10; DKFZp686E23276	aldehyde dehydrogenase 3 family, member A2
BC020757	0.436	MT1; MT1K; MGC12386	metallothionein 1G
NM_017540	0.436	FLJ00205; FLJ11715; GalNAcT10; DKFZp586H0623; pp-GalNAc-T10	UDP-N-acetyl-alpha-D-galactosamine:polypeptide N-acetylgalactosaminyltransferase 10 (GalNAc-T10)
NM_001005340	0.416	NMB; HGFIN	glycoprotein (transmembrane) nmb
AY033611	0.414	N/A	Homo sapiens placenta immunoregulatory factor PLIF mRNA, complete cds.
AB058747	0.406	Wwp4; BM-016; PRO1741; MGC10753; bA48B24.1	WW domain containing adaptor with coiled-coil
NM_015469	0.387	HSPC299; FLJ13953; MGC14553; DKFZp564D177	nipsnap homolog 3A (C. elegans)
BX538238	0.384	MALAT-1; alpha gene; metastasis associated in lung adenocarcinoma transcript 1	metastasis associated lung adenocarcinoma transcript 1 (non-coding RNA)
AB000584	0.363	PDF; MIC1; PLAB; MIC-1; NAG-1; PTGFB; GDF-15	growth differentiation factor 15
NM_005013	0.28	NEFA	nucleobindin 2

APPENDIX 2: Summary of Uniquely Regulated Genes in PC-346C Passing the 1.8 Fold Cut-off After Benjamani-Hochberg MTC

GenBank ID	Fold Change	Common Name	Description
NM_001354	7.585	DD; DD2; BABP; DDH2; HBAB; HAKRD; MCDR2; AKR1C-pseudo	aldo-keto reductase family 1, member C2 (hydroxysteroid dehydrogenase, type III)
NM_001353	5.215	C9; DD1; DDH; DDH1; H-37; MBAB; HAKRC; MGC8954; 2-ALPHA-HSD; 20-ALPHA-HSD	aldo-keto reductase family 1, member C1 (20-alpha (3-alpha)-hydroxysteroid dehydrogenase)
NM_031459	4.649	HI95; SES2; SEST2; DKFZp761M0212; DKFZp761M02121	sestrin 2
NM_000499	4.458	AHH; AHRR; CP11; CYP1; P1-450; P450-C; P450DX	cytochrome P450, family 1, subfamily A, polypeptide 1
NM_024111	3.088	MGC4504	ChaC, cation transport regulator-like 1 (E. coli)
NM_003486	3.077	E16; CD98; LAT1; 4F2LC; MPE16; hLAT1; D16S469E	solute carrier family 7 (cationic amino acid transporter, y+ system), member 5
NM_004024	3.014	ATF3	activating transcription factor 3
NM_001675	2.774	CREB2; TXREB; CREB-2; TAXREB67	activating transcription factor 4 (tax-responsive enhancer element B67)
NM_002133	2.663	HO-1; bK286B10	heme oxygenase (decycling) 1
NM_005720	2.649	ARC41; p40-ARC; p41-ARC	actin related protein 2/3 complex, subunit 1B, 41kDa
NM_002166	2.447	ID2A; ID2H; MGC26389	inhibitor of DNA binding 2, dominant negative helix-loop-helix protein
NM_031228	2.436	XAP4; RBCK1; RNF54; UBCE7IP3	chromosome 20 open reading frame 18
NM_003714	2.304	STC-2; STCRP	stanniocalcin 2
NM_012385	2.299	P8; COM1	p8 protein (candidate of metastasis 1)
NM_003376	2.124	VPF; VEGFA; MGC70609	vascular endothelial growth factor
NM_003897	2.099	DIF2; IEX1; PRG1; DIF-2; GLY96; IEX-1; IEX-1L	immediate early response 3
NM_015383	2.054	FLJ35032; RP3-328E19.1; DJ328E19.C1.1	neuroblastoma breakpoint family, member 14
NM_003763	2.03	SYN16; hsyn16; MGC90328	syntaxin 16
NM_016818	2.002	ABC8; WHITE1; MGC34313	ATP-binding cassette, sub-family G (WHITE), member 1
NM_002769	1.83	TRP1; TRY1; TRY4; TRYP1; MGC120175	protease, serine, 1 (trypsin 1)
NM_000247	0.555	PERB11.1; truncated	MHC class I polypeptide-related sequence A
NM_032356	0.551	PFAAP2; MGC14151; MGC74837	LSM domain containing 1
NM_014206	0.55	C11orf10	chromosome 11 open reading frame 10
NM_030877	0.55	NAP; P14L; PP8304; C20orf33; FLJ21108; NYD-SP19; dJ633O20.1	catenin, beta like 1
NM_031426	0.549	IBA2; FLJ12783; MGC29466; RP11-544A12.2	chromosome 9 open reading frame 58
NM_004553	0.544	NDUFS6	NADH dehydrogenase (ubiquinone) Fe-S protein 6, 13kDa (NADH-coenzyme Q reductase)
NM_078473	0.544	BLP1; MGC125813; MGC125814	TM2 domain containing 2
NM_133333	0.541	NSD2; TRX5; MMSET; REIIBP; KIAA1090	Wolf-Hirschhorn syndrome candidate 1
NM_033198	0.539	DKFZp686K20216	phosphatidylinositol glycan, class S
NM_015721	0.538	HC56; HHRF-1; DKFZP434B131; DKFZP434D174	gem (nuclear organelle) associated protein 4
NM_012412	0.535	H2AV; MGC1947; MGC10170; MGC10831	H2A histone family, member V
NM_032731	0.535	TRP14; MGC14353	thioredoxin-like 5
NM_013253	0.535	REIC	dickkopf homolog 3 (Xenopus laevis)
NM_003095	0.535	SMF	small nuclear ribonucleoprotein polypeptide F
NM_002512	0.534	puf; NDPKB; NM23B; NM23-H2; MGC111212	non-metastatic cells 2, protein (NM23B) expressed in
NM_004889	0.531	ATP5JL	ATP synthase, H+ transporting, mitochondrial F0 complex, subunit f, isoform 2
NM_003124	0.531	SPR	sepiapterin reductase (7,8-dihydrobiopterin:NADP+ oxidoreductase)
NM_014302	0.53	SSS1	Sec61 gamma subunit
NM_019896	0.529	p12	polymerase (DNA-directed), epsilon 4 (p12 subunit)
NM_004642	0.528	DOC1; ST19; DORC1; doc-1; p12DOC-1	CDK2-associated protein 1
NM_021005	0.526	ARP1; SVP40; COUPTFB; TFCOUP2; COUP-TFII; MGC117452	nuclear receptor subfamily 2, group F, member 2
NM_003198	0.526	SIII; TCEB3A	transcription elongation factor B (SIII), polypeptide 3 (110kDa, elongin A)
NM_018235	0.525	CN2; CPGL; PEPA; HsT2298; FLJ10830	CNDP dipeptidase 2 (metallopeptidase M20 family)
NM_153201	0.525	LAP1; HSC54; HSC70; HSC71; HSP71; HSP73; NIP71; HSPA10; MGC29929	heat shock 70kDa protein 8
NM_003009	0.522	selW	selenoprotein W, 1
NM_014161	0.521	HSPC071; MRP-L18	mitochondrial ribosomal protein L18
NM_004587	0.521	hES; ES130; ES/130; DKFZp586A1420	ribosome binding protein 1 homolog 180kDa (dog)
NM_005827	0.521	UGTREL1	solute carrier family 35, member B1
NM_032111	0.521	RMPL32; RPML32; MRP-L32; MGC70566	mitochondrial ribosomal protein L14
NM_014281	0.52	SIAHBP1; FIR; PUF60; RoBPI	fuse-binding protein-interacting repressor
NM_021734	0.519	DNC; MUP1; MCPHA	solute carrier family 25 (mitochondrial deoxynucleotide carrier), member 19
NM_003707	0.518	RVB1; ECP54; TIP49; NMP238; TIP49A	RuvB-like 1 (E. coli)
NM_031990	0.517	PTB; PTB2; PTB3; PTB4; pPTB; HNRPI; PTB-1; PTB-T; HNRNPI; MGC8461; MGC10830	polypyrimidine tract binding protein 1
NM_000701	0.516	MGC3285; MGC51750	ATPase, Na+/K+ transporting, alpha 1 polypeptide
NM_014317	0.515	TPT; hDPS1; MGC70953; RP13-16H11.3	trans-prenyltransferase
NM_024292	0.513	HUB1	ubiquitin-like 5
NM_001212	0.511	p32; HABP1; gC1qR; GC1QBP; SF2p32; gC1Q-R	complement component 1, q subcomponent binding protein
NM_023033	0.51	TRM8; C12orf1; YDL201w	methyltransferase like 1
NM_001384	0.508	DPH2L2	DPH2 homolog (S. cerevisiae)
NM_005175	0.508	ATP5G	ATP synthase, H+ transporting, mitochondrial F0 complex, subunit c (subunit 9), isoform 1
NM_002860	0.507	GSAS; P5CS; PYCS; MGC117316	aldehyde dehydrogenase 18 family, member A1
NM_032010	0.506	MAP5; FUTSCH; DKFZp686F1345	microtubule-associated protein 1B
NM_006758	0.506	RN; FP793; U2AF35; U2AFBP; RNU2AF1; DKFZp313J1712	U2(RNU2) small nuclear RNA auxiliary factor 1
NM_017845	0.505	FLJ20502	COMM domain containing 8
NM_006793	0.505	AOP1; MER5; AOP-1; SP-22; PRO1748; MGC24293	peroxiredoxin 3
NM_012474	0.504	UK; UMPK; TSA903	uridine-cytidine kinase 2
NM_015973	0.502	GALN; GLNN; MGC40167	galanin
NM_030928	0.501	CDT1; DUP	DNA replication factor

NM_170773	0.5	KIAA0168; DKFZp781O1747	Ras association (RalGDS/AF-6) domain family 2
NM_004092	0.499	SCEH	enoyl Coenzyme A hydratase, short chain, 1, mitochondrial
NM_000942	0.496	CYPB; SCYLP; CYP-S1; MGC2224; MGC14109	peptidylprolyl isomerase B (cyclophilin B)
NM_001686	0.494	ATPMB; ATPSB; MGC5231	ATP synthase, H+ transporting, mitochondrial F1 complex, beta polypeptide
NM_018285	0.491	BRMS2; MRPS4; C15orf12; FLJ10968; DKFZp586L0118	IMP3, U3 small nucleolar ribonucleoprotein, homolog (yeast)
NM_002004	0.491	FPS	farnesyl diphosphate synthase (farnesyl pyrophosphate synthetase, dimethylallyltranstransferase)
NM_016497	0.49	CDA09; MRP64; bMRP64; HSPC241	mitochondrial ribosomal protein L51
NM_015969	0.488	RPMS17; HSPC011; MRP-S17	mitochondrial ribosomal protein S17
NM_005826	0.485	HNRNPR; hnRNP-R	heterogeneous nuclear ribonucleoprotein R
NM_173794	0.484	MGC51029	FUN14 domain containing 1
NM_007262	0.483	DJ1; DJ-1; FLJ27376	Parkinson disease (autosomal recessive, early onset) 7
NM_005742	0.482	P5; ERP5; TXNDC7	protein disulfide isomerase family A, member 6
NM_003286	0.482	TOPI	topoisomerase (DNA) I
NM_000224	0.482	K18; CYK18	keratin 18
NM_145701	0.481	HEPP; FLJ20764; MGC19517	cell division cycle associated 4
NM_018101	0.481	BOR; FLJ10468; FLJ12042	cell division cycle associated 8
NM_006904	0.481	HYRC; p350; DNAPK; DNPK1; HYRC1; XRCC7	protein kinase, DNA-activated, catalytic polypeptide
NM_003311	0.48	IPL; BRW1C; BWR1C; HLDA2; TSSC3	pleckstrin homology-like domain, family A, member 2
NM_053056	0.479	BCL1; PRAD1; U21B31; D11S287E	cyclin D1
NM_005003	0.479	ACP; SDAP; MGC65095	NADH dehydrogenase (ubiquinone) 1, alpha/beta subcomplex, 1, 8kDa
NM_020182	0.477	STAG1; PMEPA1	transmembrane, prostate androgen induced RNA
NM_020186	0.472	DC11	ACN9 homolog (S. cerevisiae)
NM_003676	0.472	MLD; DEGS; DES1; Des-1; FADS7; MIG15; MGC5079	degenerative spermatocyte homolog 1, lipid desaturase (Drosophila)
NM_016397	0.469	TH1; NELF-C; NELF-D; HSPC130	TH1-like (Drosophila)
NM_005956	0.469	MTHFC; MTHFD	methylenetetrahydrofolate dehydrogenase (NADP+ dependent) 1, methenyltetrahydrofolate cyclohydrolase
NM_004906	0.468	MGC3925; KIAA0105; DKFZp686F20131	Wilms tumor 1 associated protein
NM_025109	0.466	FLJ22865	myosin head domain containing 1
NM_003746	0.464	LC8; PIN; DLC1; DLC8; LC8a; DNCL1; hdlc1; DNCLC1; MGC126137; MGC126138	dynein, light chain, LC8-type 1
NM_012459	0.463	DDP2; TIM8B; MGC102866; MGC117373	translocase of inner mitochondrial membrane 8 homolog B (yeast)
NM_013442	0.463	SLP-2; HSPC108	stomatin (EPB72)-like 2
NM_006600	0.462	HNUDC; MNUDC; NPD011	nuclear distribution gene C homolog (A. nidulans)
NM_016185	0.46	ARM2; HN1A	hematological and neurological expressed 1
NM_013237	0.457	PX19; PRELI; CGI-106; MGC87972	px19-like protein
NM_001436	0.456	FIB; FLRN; RNU3IP1	fibrillarin
NM_013300	0.455	HSU79274	protein predicted by clone 23733
NM_001011	0.455	RPS7	ribosomal protein S7
NM_018087	0.452	NDC1; FLJ10407; FLJ12556; FLJ34120; RP4-654H19.1	transmembrane protein 48
NM_013410	0.452	AK3; AK4	adenylate kinase 3-like 1
NM_002914	0.451	A1; RFC40; MGC3665	replication factor C (activator 1) 2, 40kDa
NM_153719	0.448	p62; MGC841; FLJ20822; DKFZp547L134	nucleoporin 62kDa
NM_012341	0.447	NGB; CRFG; FLJ10686; FLJ10690	GTP binding protein 4
NM_003681	0.447	PKH; PNK; C21orf97	pyridoxal (pyridoxine, vitamin B6) kinase
NM_001769	0.446	BA2; P24; GIG2; MIC3; MRP-1; BTCC-1; DRAP-27; TSPAN29	CD9 antigen (p24)
NM_017647	0.446	EPCS3; FLJ20062	FtsJ homolog 3 (E. coli)
NM_016058	0.445	CGI-121	CGI-121 protein
NM_014214	0.44	IMPA2	inositol(myo)-1(or 4)-monophosphatase 2
NM_017971	0.438	L20mt; MGC4779; MGC74465	mitochondrial ribosomal protein L20
NM_003094	0.437	SME	small nuclear ribonucleoprotein polypeptide E
NM_030810	0.436	ERP46; UNQ364; EndoPDI; MGC3178	thioredoxin domain containing 5
NM_000356	0.435	MFD1; treacle	Treacher Collins-Franceschetti syndrome 1
NM_001888	0.434	THBP; DFNA40	crystallin, mu
NM_004552	0.432	NDUFS5	NADH dehydrogenase (ubiquinone) Fe-S protein 5, 15kDa (NADH-coenzyme Q reductase)
NM_002128	0.428	HMG1; HMG3; SBP-1; DKFZp686A04236	high-mobility group box 1
NM_002823	0.426	TMSA; MGC104802	prothymosin, alpha (gene sequence 28)
NM_006431	0.424	CCTB; 99D8.1; PRO1633; CCT-beta; TCP-1-beta	chaperonin containing TCP1, subunit 2 (beta)
NM_016059	0.421	CYPL1; hCyPX; MGC678; PPIase; CGI-124	peptidylprolyl isomerase (cyclophilin)-like 1
NM_032758	0.419	INI; MGC1346; SF3b14b; bK223H9.2	PHD finger protein 5A
NM_032997	0.418	KNTC2AP; HZwint-1	ZW10 interactor
NM_018946	0.418	SAS	N-acetylneuraminic acid synthase (sialic acid synthase)
NM_001761	0.412	FBX1; FBXO1	cyclin F
NM_003579	0.411	HR54; hHR54; RAD54A; hRAD54	RAD54-like (S. cerevisiae)
NM_001269	0.411	CHC1; RCC1-I	regulator of chromosome condensation 1
NM_005782	0.408	ALY; BEF	THO complex 4
NM_016570	0.403	PTX1; CDA14; Erv41; cd002; MGC111152	PTX1 protein
NM_134269	0.403	SMTN	smoothelin
NM_005659	0.402	UFD1	ubiquitin fusion degradation 1 like (yeast)
NM_004814	0.402	SFP38; SPF38; PRP8BP; HPRP8BP; PRPF8BP; RP11-490K7.3	WD repeat domain 57 (U5 snRNP specific)
NM_017760	0.4	MTB; CAP-G2; hCAP-G2; FLJ20311	leucine zipper protein 5
NM_002629	0.399	PGAMA	phosphoglycerate mutase 1 (brain)
NM_004640	0.395	D6S81E	HLA-B associated transcript 1
NM_032231	0.393	FLJ22875	family with sequence similarity 96, member A
NM_006088	0.392	TUBB2	tubulin, beta 2C

NM_012394	0.391	PFD2	prefoldin 2
NM_007080	0.39	YDR378C	LSM6 homolog, U6 small nuclear RNA associated (S. cerevisiae)
NM_001096	0.39	ATPCL; CLATP	ATP citrate lyase
NM_000240	0.389	MAOA	monoamine oxidase A
NM_005387	0.384	ADIR2; NUP196	nucleoporin 98kDa
NM_016050	0.384	L11mt; CGI-113; MGC111024	mitochondrial ribosomal protein L11
NM_000269	0.383	AWD; GAAD; NM23; NDPKA; NM23-H1	non-metastatic cells 1, protein (NM23A) expressed in
NM_005729	0.383	CYP3; Cyp-D; FLJ90798; MGC117207	peptidylprolyl isomerase F (cyclophilin F)
NM_001363	0.379	DKC; NAP57; NOLA4; XAP101; dyskerin	dyskeratosis congenita 1, dyskerin
NM_032704	0.379	bcm948; MGC10851; MGC14580	tubulin, alpha 6
NM_032636	0.378	DDA3; FP3214; MGC1780; RP11-297O4.2	proline/serine-rich coiled-coil 1
NM_016395	0.377	B-IND1; HSPC121	protein tyrosine phosphatase-like A domain containing 1
NM_005381	0.376	C23; FLJ45706	nucleolin
NM_021237	0.375	SELK; HSPC030; HSPC297; MGC17057	selenoprotein K
NM_002787	0.375	MU; HC3; PSC2; PMSA2	proteasome (prosome, macropain) subunit, alpha type, 2
NM_001618	0.374	PARP; PPOL; ADPRT; ADPRT1; PARP-1; pADPRT-1	poly (ADP-ribose) polymerase family, member 1
NM_007280	0.372	5730547N13Rik	Opa interacting protein 5
NM_014463	0.37	SMX4; USS2; YLR438C	LSM3 homolog, U6 small nuclear RNA associated (S. cerevisiae)
NM_004343	0.368	RO; SSA; cC1qR	calreticulin
NM_013285	0.366	NGP1; Ngp-1; FLJ40906; HUMAUANTIG; dJ423B22.6	guanine nucleotide binding protein-like 2 (nucleolar)
NM_006708	0.364	GLYI	glyoxalase I
NM_022044	0.36	AP000553.C22.4	stromal cell-derived factor 2-like 1
NM_002786	0.36	NU; HC2; PROS30; MGC1667; MGC14542; MGC14575; MGC14751; MGC21459; MGC22853; MGC23915	proteasome (prosome, macropain) subunit, alpha type, 1
NM_001379	0.359	DNMT; MCMT; CXXC9; MGC104992	DNA (cytosine-5-)-methyltransferase 1
NM_002539	0.358	ODC1	ornithine decarboxylase 1
NM_144998	0.353	E3; MGC14480	stimulated by retinoic acid 13 homolog (mouse)
NM_058216	0.351	RAD51L2; MGC104277	RAD51 homolog C (S. cerevisiae)
NM_004499	0.351	ABBP1	heterogeneous nuclear ribonucleoprotein A/B
NM_175698	0.349	SSX; HD21; MGC3884; MGC15364; MGC119055; HOM-MEL-40	synovial sarcoma, X breakpoint 2
NM_000465	0.34	BARD1	BRCA1 associated RING domain 1
NM_006006	0.338	PLZF; ZNF145	zinc finger and BTB domain containing 16
NM_006347	0.338	CYPH; CYP-20; MGC5016; USA-CYP; SnuCyp-20	peptidyl prolyl isomerase H (cyclophilin H)
NM_079423	0.336	ESMLC; LC17A; LC17B; MLC1SM; MLC3NM; MLC3SM; LC17-GI; LC17-NM	myosin, light polypeptide 6, alkali, smooth muscle and non-muscle
NM_003096	0.336	SMG; MGC117317	small nuclear ribonucleoprotein polypeptide G
NM_005313	0.336	P58; ERp57; ERp60; ERp61; GRP57; GRP58; PI-PLC; HsT17083	protein disulfide isomerase family A, member 3
NM_003711	0.335	LPP1; PAP2; LLP1a; PAP-2a; PAP2a2; PAPalpha1; PAP2alpha2	phosphatidic acid phosphatase type 2A
NM_001239	0.329	CAK; p34; p37	cyclin H
NM_006027	0.327	HEX1; hExoI	exonuclease 1
NM_004153	0.324	ORC1; PARC1; HSORC1	origin recognition complex, subunit 1-like (yeast)
NM_021149	0.321	CLP; FLJ43657; MGC19733	coactosin-like 1 (Dictyostelium)
NM_005804	0.321	BAT1; DDXL; URH49; MGC8417; MGC18203	DEAD (Asp-Glu-Ala-Asp) box polypeptide 39
NM_005573	0.32	LMN; LMN2; LMNB; MGC111419	lamin B1
NM_012310	0.318	KIF4; KIF4-G1; HSA271784	kinesin family member 4A
NM_005348	0.316	HSPN; LAP2; HSP86; HSPC1; Hsp89; Hsp90; HSP90A; HSPCAL1; FLJ31884	heat shock 90kDa protein 1, alpha
NM_004219	0.315	EAP1; PTTG; HPTTG; TUTR1; SECURIN; MGC126883	pituitary tumor-transforming 1
NM_014754	0.315	PSSA; KIAA0024	phosphatidylserine synthase 1
NM_022116	0.311	FIGNL1	fidgetin-like 1
NM_021953	0.311	MPP2; HFH11; HNF-3; INS-1; MPP-2; PIG29; FKHL16; FOXM1B; HFH-11; TRIDENT; MPHOSPH2	forkhead box M1
NM_024079	0.308	MGC2840	asparagine-linked glycosylation 8 homolog (yeast, alpha-1,3-glucosyltransferase)
NM_002689	0.307	FLJ21662	polymerase (DNA directed), alpha 2 (70kD subunit)
NM_016326	0.305	C32; CKLF1; CKLF2; CKLF3; CKLF4; UCK-1; HSPC224	chemokine-like factor
NM_016310	0.299	C11; RPC10; RPC11; hRPC11; C11-RNP3	polymerase (RNA) III (DNA directed) polypeptide K, 12.3 kDa
NM_021177	0.296	G7b; snRNP; C6orf28; YBL026W	LSM2 homolog, U6 small nuclear RNA associated (S. cerevisiae)
NM_014762	0.291	KIAA0018; SELADIN1; Nbla03646; seladin-1	24-dehydrocholesterol reductase
NM_024324	0.288	MGC11256; DKFZp667O055	cysteine-rich with EGF-like domains 2
NM_004048	0.286	B2M	beta-2-microglobulin
NM_001539	0.286	DJ-2; DjA1; HDJ2; HSDJ; HSJ2; HSPF4; hDJ-2	DnaJ (Hsp40) homolog, subfamily A, member 1
NM_018454	0.285	LNP; ANKT; SAPL; BM037; Q0310; FLJ13421; PRO0310p1	nucleolar and spindle associated protein 1
NM_013402	0.27	D5D; TU12; FADS6; FADSD5; LLCDL1; FLJ90273; BC269730_2	fatty acid desaturase 1
NM_022154	0.265	BIGM103; LZT-Hs6	solute carrier family 39 (zinc transporter), member 8
NM_020244	0.265	CPT; CPT1	choline phosphotransferase 1
NM_007274	0.256	ACT; ACH1; BACH; LACH1; hBACH; CTE-II; MGC1126; RP1-120G22.10	acyl-CoA thioesterase 7
NM_003981	0.255	MGC1671; MGC3669	protein regulator of cytokinesis 1
NM_006010	0.228	ARP	arginine-rich, mutated in early stage tumors
NM_018154	0.223	CIA-II; FLJ10604	ASF1 anti-silencing function 1 homolog B (S. cerevisiae)
NM_022132	0.218	MCCB	methylcrotonoyl-Coenzyme A carboxylase 2 (beta)
NM_032637	0.214	FBL1; FLB1; FBXL1; MGC1366	S-phase kinase-associated protein 2 (p45)
NM_004911	0.203	ERP70; ERP72	protein disulfide isomerase family A, member 4
NM_005551	0.202	hK2; KLK2A2; MGC12201	kallikrein 2, prostatic
NM_003299	0.201	ECGP; GP96; GRP94	tumor rejection antigen (gp96) 1
NM_002946	0.2	REPA2; RPA32	replication protein A2, 32kDa
NM_001316	0.196	CAS; CSE1; XPO2; MGC117283; MGC130036; MGC130037	CSE1 chromosome segregation 1-like (yeast)

NM_006601	0.196	P23; TEBP	prostaglandin E synthase 3 (cytosolic)
NM_003920	0.187	TIM; TIM1; hTIM	timeless homolog (Drosophila)
NM_001274	0.164	CHK1	CHK1 checkpoint homolog (S. pombe)
NM_001067	0.16	TOP2; TP2A	topoisomerase (DNA) II alpha 170kDa
NM_138555	0.157	CHO1; KNSL5; MKLP1; MKLP-1	kinesin family member 23
NM_021992	0.0649	TMSNB	thymosin-like 8
NM_022049	0.0615	STRG	G-protein coupled receptor 88

APPENDIX 3: Summary of Commonly Regulated Genes in LNCaP cells Passing the 1.8 Fold Cut-off After Benjamani-Hochberg MTC

GenBank ID	Fold Change	Common Name	Description
NM_005980	6.232	MIG9	S100 calcium binding protein P
NM_004083	2.114	CHOP; CEBPZ; CHOP10; GADD153; MGC4154	DNA-damage-inducible transcript 3
NM_001018073	2.073	PEPCK; PEPCK2; PEPCK-M	phosphoenolpyruvate carboxykinase 2 (mitochondrial)
NM_019096	2.03	MGC74725	GTP binding protein 2
NM_021158	1.992	NIPK; SINK; TRB3; SKIP3; C20orf97	tribbles homolog 3 (Drosophila)
NM_005194	1.824	LAP; CRP2; TCF5; IL6DBP; NF-IL6; MGC32080; C/EBP-beta	CCAAT/enhancer binding protein (C/EBP), beta
NM_000389	1.821	P21; CIP1; SDI1; WAF1; CAP20; CDKN1; MDA-6; p21CIP1	cyclin-dependent kinase inhibitor 1A (p21, Cip1)
NM_016095	0.551	Pfs2; HSPC037	DNA replication complex GINS protein PSF2
NM_023938	0.548	SARG; MGC2742; MGC4309; FLJ36507; DKFZp666H2010	chromosome 1 open reading frame 116
NM_004462	0.545	SS; SQS; DGPT; ERG9	farnesyl-diphosphate farnesyltransferase 1
NM_006607	0.545	PTTG2	pituitary tumor-transforming 2
NM_022061	0.545	RPL17L; RPML26; MRP-L26	mitochondrial ribosomal protein L17
NM_003600	0.544	AIK; ARK1; AURA; BTAK; STK15; MGC34538	serine/threonine kinase 6
NM_005566	0.544	LDH1; PIG19	lactate dehydrogenase A
NM_001424	0.54	XMP; MGC9056	epithelial membrane protein 2
NM_001010850	0.538	TLS; FUS1; FUS-CHOP	fusion (involved in t(12;16) in malignant liposarcoma)
NM_015934	0.537	NOP5/NOP58; HSPC120	nucleolar protein NOP5/NOP58
NM_002882	0.529	MGC88701	RAN binding protein 1
NM_005225	0.525	RBP3; E2F-1; RBBP3	E2F transcription factor 1
NM_001033	0.525	R1; RR1; RIR1	ribonucleotide reductase M1 polypeptide
NM_020548	0.517	ACBP; ACBD1; MGC70414	diazepam binding inhibitor (GABA receptor modulator, acyl-Coenzyme A binding protein)
NM_006101	0.517	HEC; HEC1	kinetochore associated 2
NM_006845	0.514	MCAK; KNSL6	kinesin family member 2C
NM_015190	0.513	JDD1; SB73; KIAA0974	DnaJ (Hsp40) homolog, subfamily C, member 9
NM_002466	0.512	BMYB; MGC15600	v-myb myeloblastosis viral oncogene homolog (avian)-like 2
NM_014176	0.511	PIG50; HSPC150	ubiquitin-conjugating enzyme E2T (putative)
NM_006579	0.508	CPX; CHO2; CPXD; CDPX2	emopamil binding protein (sterol isomerase)
NM_002388	0.506	HCC5; P1.h; RLFB; MGC1157; P1-MCM3	MCM3 minichromosome maintenance deficient 3 (S. cerevisiae)
NM_006527	0.502	HBP	stem-loop (histone) binding protein
NM_006739	0.5	CDC46; MGC5315; P1-CDC46	MCM5 minichromosome maintenance deficient 5, cell division cycle 46 (S. cerevisiae)
NM_002452	0.497	MTH1	nudix (nucleoside diphosphate linked moiety X)-type motif 1
NM_013282	0.497	Np95; ICBP90; RNF106; huNp95; FLJ21925	ubiquitin-like, containing PHD and RING finger domains, 1
NM_000270	0.496	PNP; PRO1837; MGC117396; MGC125915; MGC125916	nucleoside phosphorylase
NM_031299	0.467	GRCC8; TOME-1; MGC2577	cell division cycle associated 3
NM_006167	0.458	NKX3A; NKX3.1	NK3 transcription factor related, locus 1 (Drosophila)
NM_002106	0.445	H2AZ; H2A.z; H2A/z; MGC117173	H2A histone family, member Z
NM_005733	0.439	MKLP2; RAB6KIFL	kinesin family member 20A
NM_018685	0.437	Scraps; ANILLIN; DKFZp779A055	anillin, actin binding protein (scraps homolog, Drosophila)
NM_015415	0.433	MGC125752; MGC125753; DKFZP564B167	brain protein 44
NM_002592	0.428	MGC8367	proliferating cell nuclear antigen
NM_006082	0.425	K-ALPHA-1	tubulin, alpha, ubiquitous
NM_002266	0.42	QIP2; RCH1; IPOA1; SRP1alpha	karyopherin alpha 2 (RAG cohort 1, importin alpha 1)
NM_003504	0.419	CDC45; CDC45L2; PORC-PI-1	CDC45 cell division cycle 45-like (S. cerevisiae)
NM_006461	0.406	MAP126; DEEPEST; hMAP126	sperm associated antigen 5
NM_012112	0.405	DIL2; p100; DIL-2; HCTP4; FLS353; HCA519; REPP86; C20orf1; C20orf2; GD:C20orf1	TPX2, microtubule-associated, homolog (Xenopus laevis)
NM_018492	0.403	SPK; TOPK; Nori-3; FLJ14385	PDZ binding kinase
NM_002105	0.394	H2AX; H2A.X; H2A/X	H2A histone family, member X
NM_005656	0.394	PRSS10	transmembrane protease, serine 2
NM_018456	0.389	U19; BM040; TRAITS	ELL associated factor 2
NM_005563	0.388	Lag; SMN; OP18; PP17; PP19; PR22; LAP18	stathmin 1/oncoprotein 18
NM_004111	0.382	MF1; RAD2; FEN-1	flap structure-specific endonuclease 1
NM_005192	0.378	KAP; CDI1; CIP2; KAP1; FLJ25787; MGC70625	cyclin-dependent kinase inhibitor 3 (CDK2-associated dual specificity phosphatase)
NM_004701	0.378	HsT17299	cyclin B2
NM_007019	0.371	UBCH10; dJ447F3.2	ubiquitin-conjugating enzyme E2C
NM_004595	0.37	SRS; SpS; MRSR; SPMSY	spermine synthase
NM_001030047	0.357	APS; PSA; hK3; KLK2A1	kallikrein 3, (prostate specific antigen)
NM_002129	0.352	HMG2	high-mobility group box 2
NM_006342	0.345	ERIC1; MGC117382	transforming, acidic coiled-coil containing protein 3
NM_004526	0.327	BM28; CCNL1; CDCL1; cdc19; D3S3194; MITOTIN; KIAA0030; MGC10606	MCM2 minichromosome maintenance deficient 2, mitotin (S. cerevisiae)
NM_004217	0.326	AIK2; AIM1; ARK2; AurB; IPL1; STK5; AIM-1; STK12	aurora kinase B
NM_006397	0.3	JUNB; RNHL; RNHIA; RNASEHI	ribonuclease H2, large subunit
NM_001826	0.298	CKS1; ckshs1; PNAS-16; PNAS-18	CDC28 protein kinase regulatory subunit 1B
NM_016359	0.296	LNP; ANKT; SAPL; BM037; Q0310; FLJ13421; PRO0310p1	nucleolar and spindle associated protein 1

NM_004117	0.288	P54; FKBP51; FKBP54; PPIase; Ptg-10; MGC111006	FK506 binding protein 5
NM_031966	0.283	CCNB	cyclin B1
NM_005916	0.271	MCM2; CDC47; P85MCM; P1CDC47; PNAS-146; CDABP0042; P1.1-MCM3	MCM7 minichromosome maintenance deficient 7 (S. cerevisiae)
NM_001012270	0.265	API4; EPR-1	baculoviral IAP repeat-containing 5 (survivin)
NM_001005413	0.264	KNTC2AP; HZwint-1	ZW10 interactor
NM_024629	0.255	KLIP1; FLJ23468	MLF1 interacting protein
NM_001071	0.248	TS; TMS; TSase; HsT422; MGC88736	thymidylate synthetase
NM_001255	0.24	p55CDC; MGC102824; bA276H19.3	CDC20 cell division cycle 20 homolog (S. cerevisiae)
NM_080668	0.23	MGC16386	cell division cycle associated 5
NM_001786	0.208	CDK1; MGC111195; DKFZp686L20222	cell division cycle 2, G1 to S and G2 to M
NM_003258	0.202	TK2	thymidine kinase 1, soluble
NM_003542	0.174	H4/g; H4FG; dJ221C16.1	histone 1, H4c

APPENDIX 4: Summary of Commonly Regulated Genes in PC-346C cells Passing the 1.8 Fold Cut-off After Benjamani-Hochberg MTC

GenBank ID	Fold Change	Common Name	Description
NM_021158	6.797	NIPK; SINK; TRB3; SKIP3; C20orf97	tribbles homolog 3 (Drosophila)
NM_004083	5	CHOP; CEBPZ; CHOP10; GADD153; MGC4154	DNA-damage-inducible transcript 3
NM_005194	3.683	LAP; CRP2; TCF5; IL6DBP; NF-IL6; MGC32080; C/EBP-beta	CCAAT/enhancer binding protein (C/EBP), beta
NM_019096	3.148	MGC74725	GTP binding protein 2
NM_005980	2.835	MIG9	S100 calcium binding protein P
NM_078467	2.361	P21; CIP1; SDI1; WAF1; CAP20; CDKN1; MDA-6; p21CIP1	cyclin-dependent kinase inhibitor 1A (p21, Cip1)
NM_004563	1.901	PEPCK; PEPCK2; PEPCK-M	phosphoenolpyruvate carboxykinase 2 (mitochondrial)
NM_006607	0.552	PTTG2	pituitary tumor-transforming 2
NM_006167	0.536	NKX3A; NKX3.1	NK3 transcription factor related, locus 1 (Drosophila)
NM_004960	0.529	TLS; FUS1; FUS-CHOP	fusion (involved in t(12;16) in malignant liposarcoma)
NM_022061	0.504	RPL17L; RPML26; MRP-L26	mitochondrial ribosomal protein L17
NM_001424	0.474	XMP; MGC9056	epithelial membrane protein 2
NM_005656	0.473	PRSS10	transmembrane protease, serine 2
NM_023938	0.465	SARG; MGC2742; MGC4309; FLJ36507; DKFZp666H2010	chromosome 1 open reading frame 116
NM_002452	0.454	MTH1	nudix (nucleoside diphosphate linked moiety X)-type motif 1
NM_006739	0.44	CDC46; MGC5315; P1-CDC46	MCM5 minichromosome maintenance deficient 5, cell division cycle 46 (S. cerevisiae)
NM_002882	0.417	MGC88701	RAN binding protein 1
NM_007019	0.416	UBCH10; dJ447F3.2	ubiquitin-conjugating enzyme E2C
NM_006397	0.414	JUNB; RNHL; RNHIA; RNASEHI	ribonuclease H2, large subunit
NM_003504	0.408	CDC45; CDC45L2; PORC-PI-1	CDC45 cell division cycle 45-like (S. cerevisiae)
NM_031299	0.389	GRCC8; TOME-1; MGC2577	cell division cycle associated 3
NM_015934	0.383	NOP5/NOP58; HSPC120	nucleolar protein NOP5/NOP58
NM_004111	0.368	MF1; RAD2; FEN-1	flap structure-specific endonuclease 1
NM_006527	0.351	HBP	stem-loop (histone) binding protein
NM_006579	0.343	CPX; CHO2; CPXD; CDPX2	emopamil binding protein (sterol isomerase)
NM_018456	0.341	U19; BM040; TRAITS	ELL associated factor 2
NM_004217	0.331	AIK2; AIM1; ARK2; AurB; IPL1; STK5; AIM-1; STK12	aurora kinase B
NM_018492	0.322	SPK; TOPK; Nori-3; FLJ14385	PDZ binding kinase
NM_020548	0.322	ACBP; ACBD1; MGC70414	diazepam binding inhibitor (GABA receptor modulator, acyl-Coenzyme A binding protein)
NM_014176	0.315	PIG50; HSPC150	ubiquitin-conjugating enzyme E2T (putative)
NM_005225	0.299	RBP3; E2F-1; RBBP3	E2F transcription factor 1
NM_004462	0.287	SS; SQS; DGPT; ERG9	farnesyl-diphosphate farnesyltransferase 1
NM_006342	0.276	ERIC1; MGC117382	transforming, acidic coiled-coil containing protein 3
NM_004595	0.27	SRS; SpS; MRSR; SPMSY	spermine synthase
NM_001033	0.27	R1; RR1; RIR1	ribonucleotide reductase M1 polypeptide
NM_018685	0.27	Scraps; ANILLIN; DKFZp779A055	anillin, actin binding protein (scraps homolog, Drosophila)
NM_006082	0.266	K-ALPHA-1	tubulin, alpha, ubiquitous
NM_033379	0.243	CDK1; MGC111195; DKFZp686L20222	cell division cycle 2, G1 to S and G2 to M
NM_002388	0.238	HCC5; P1.h; RLFB; MGC1157; P1-MCM3	MCM3 minichromosome maintenance deficient 3 (S. cerevisiae)
NM_001648	0.235	APS; PSA; hK3; KLK2A1	kallikrein 3, (prostate specific antigen)
NM_001826	0.228	CKS1; ckshs1; PNAS-16; PNAS-18	CDC28 protein kinase regulatory subunit 1B
NM_006461	0.218	MAP126; DEEPEST; hMAP126	sperm associated antigen 5
NM_005733	0.216	MKLP2; RAB6KIFL	kinesin family member 20A
NM_016095	0.213	Pfs2; HSPC037	DNA replication complex GINS protein PSF2
NM_002266	0.202	QIP2; RCH1; IPOA1; SRP1alpha	karyopherin alpha 2 (RAG cohort 1, importin alpha 1)
NM_002466	0.197	BMYB; MGC15600	v-myb myeloblastosis viral oncogene homolog (avian)-like 2
NM_002105	0.196	H2AX; H2A.X; H2A/X	H2A histone family, member X
NM_015415	0.195	MGC125752; MGC125753; DKFZP564B167	brain protein 44
NM_002106	0.194	H2AZ; H2A.z; H2A/z; MGC117173	H2A histone family, member Z

NM_003258	0.194	TK2	thymidine kinase 1, soluble
NM_006845	0.192	MCAK; KNSL6	kinesin family member 2C
NM_000270	0.192	PNP; PRO1837; MGC117396; MGC125915; MGC125916	nucleoside phosphorylase
NM_003542	0.186	H4/g; H4FG; dJ221C16.1	histone 1, H4c
NM_015190	0.18	JDD1; SB73; KIAA0974	DnaJ (Hsp40) homolog, subfamily C, member 9
NM_002129	0.179	HMG2	high-mobility group box 2
NM_012112	0.174	DIL2; p100; DIL-2; HCTP4; FLS353; HCA519; REPP86; C20orf1; C20orf2;	TPX2, microtubule-associated, homolog (Xenopus laevis)
NM_005916	0.173	MCM2; CDC47; P85MCM; P1CDC47; PNAS-146; CDABP0042; P1.1-MCM	MCM7 minichromosome maintenance deficient 7 (S. cerevisiae)
NM_080668	0.154	MGC16386	cell division cycle associated 5
NM_005566	0.152	LDH1; PIG19	lactate dehydrogenase A
NM_001071	0.146	TS; TMS; TSase; HsT422; MGC88736	thymidylate synthetase
NM_013282	0.14	Np95; ICBP90; RNF106; huNp95; FLJ21925	ubiquitin-like, containing PHD and RING finger domains, 1
NM_004701	0.135	HsT17299	cyclin B2
NM_007057	0.13	KNTC2AP; HZwint-1	ZW10 interactor
NM_004526	0.124	BM28; CCNL1; CDCL1; cdc19; D3S3194; MITOTIN; KIAA0030; MGC1060	MCM2 minichromosome maintenance deficient 2, mitotin (S. cerevisiae)
NM_005192	0.123	KAP; CDI1; CIP2; KAP1; FLJ25787; MGC70625	cyclin-dependent kinase inhibitor 3 (CDK2-associated dual specificity phosphatase)
NM_003600	0.116	AIK; ARK1; AURA; BTAK; STK15; MGC34538	serine/threonine kinase 6
NM_031966	0.112	CCNB	cyclin B1
NM_002592	0.112	MGC8367	proliferating cell nuclear antigen
NM_005563	0.106	Lag; SMN; OP18; PP17; PP19; PR22; LAP18	stathmin 1/oncoprotein 18
NM_006101	0.104	HEC; HEC1	kinetochore associated 2
NM_001255	0.0929	p55CDC; MGC102824; bA276H19.3	CDC20 cell division cycle 20 homolog (S. cerevisiae)
NM_004117	0.0882	P54; FKBP51; FKBP54; PPIase; Ptg-10; MGC111006	FK506 binding protein 5
NM_001168	0.0866	API4; EPR-1	baculoviral IAP repeat-containing 5 (survivin)
NM_016359	0.0747	LNP; ANKT; SAPL; BM037; Q0310; FLJ13421; PRO0310p1	nucleolar and spindle associated protein 1
NM_024629	0.0569	KLIP1; FLJ23468	MLF1 interacting protein